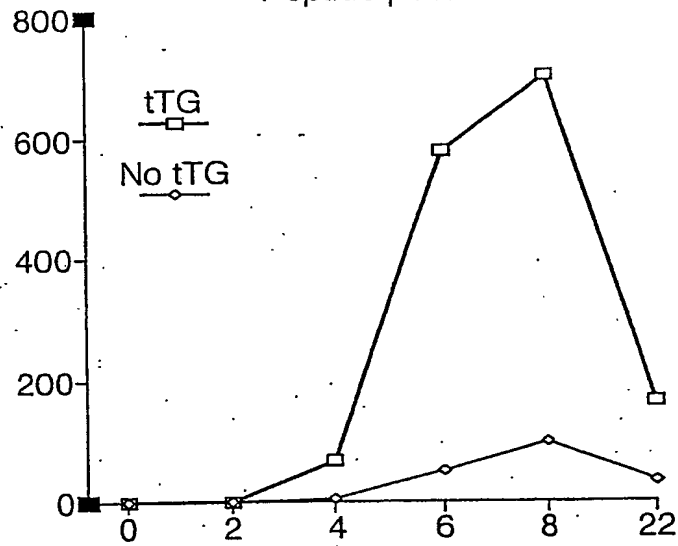
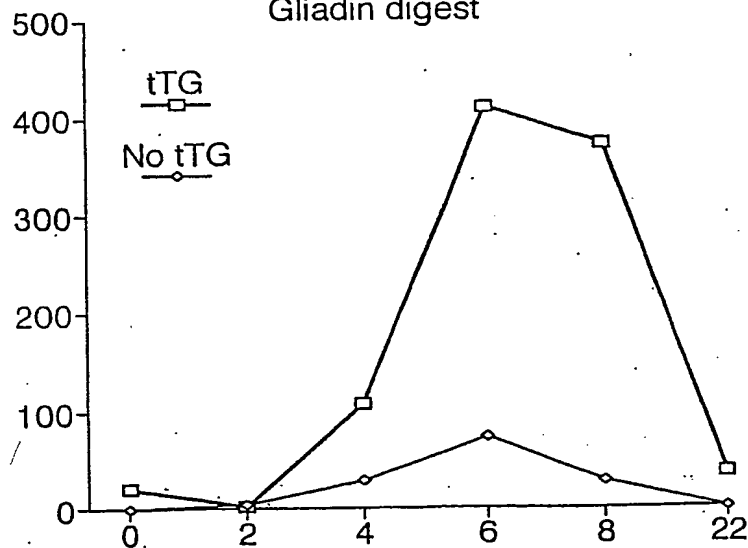


Fig. 1a.

Peptide pool 3



Gliadin digest



BEST AVAILABLE COPY

Fig.1b.

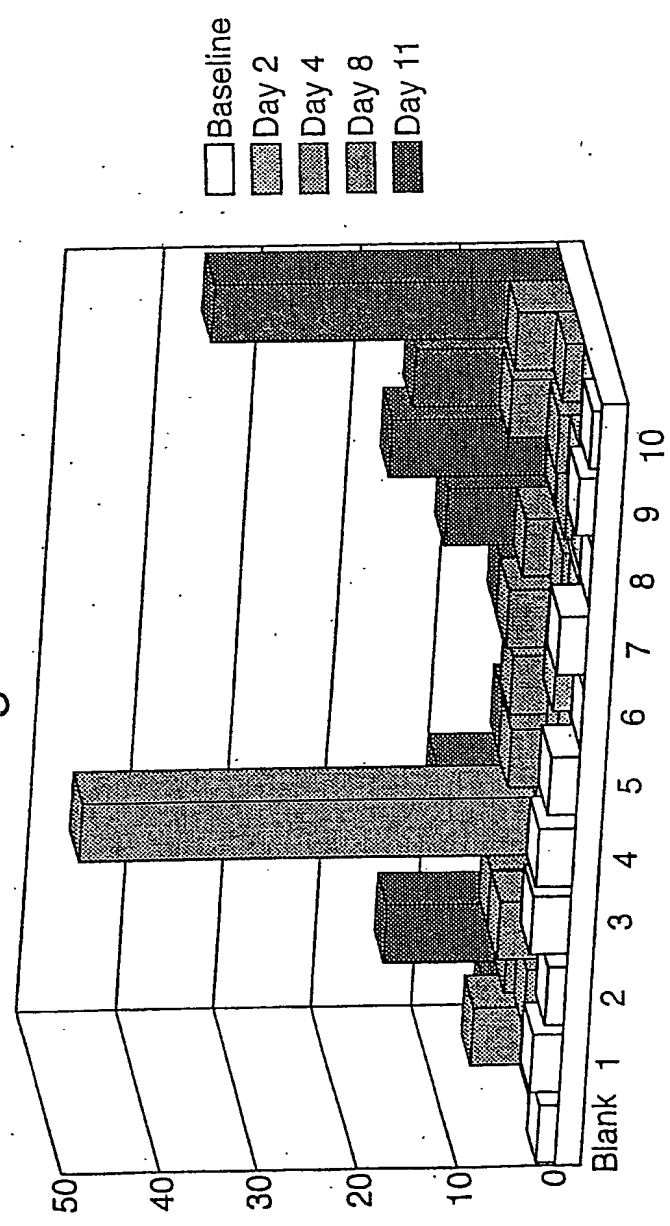


Fig.2a.

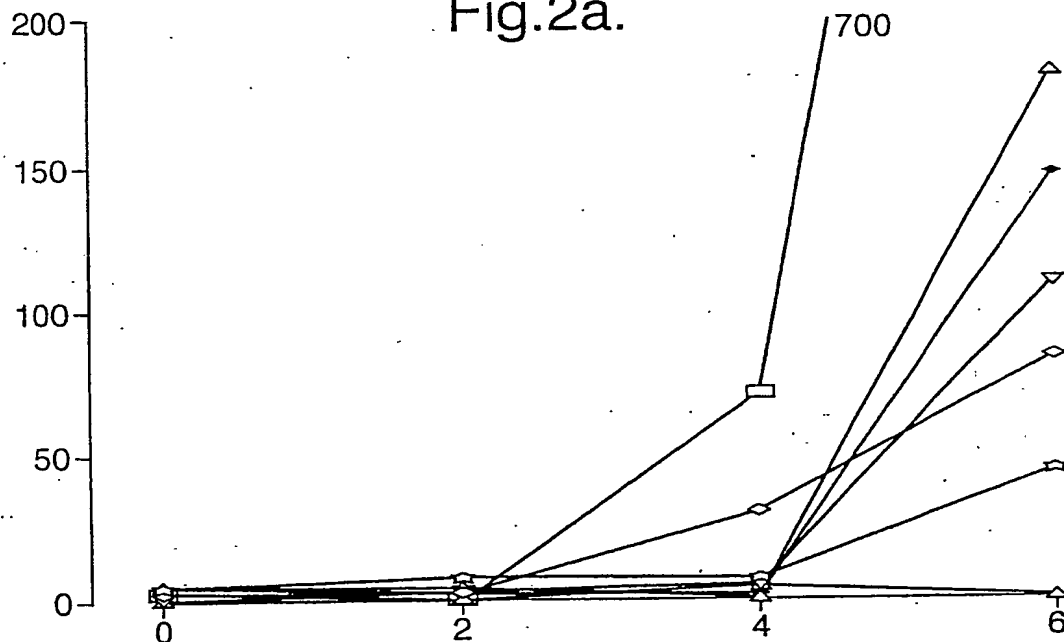
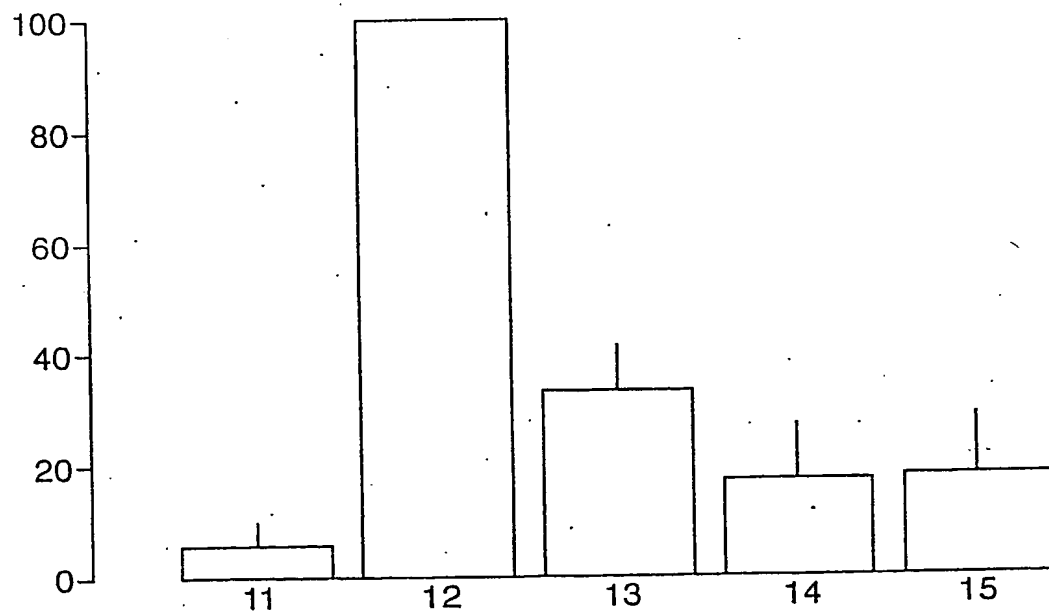


Fig.2b.



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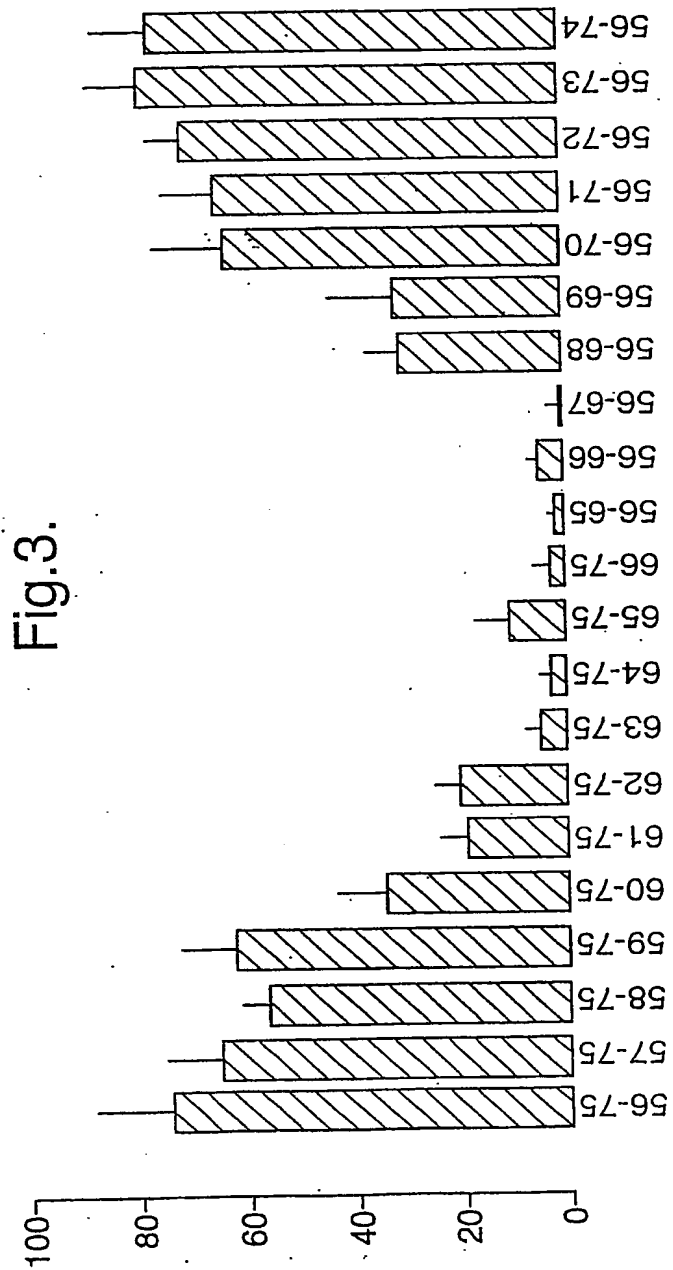


Fig.4a.

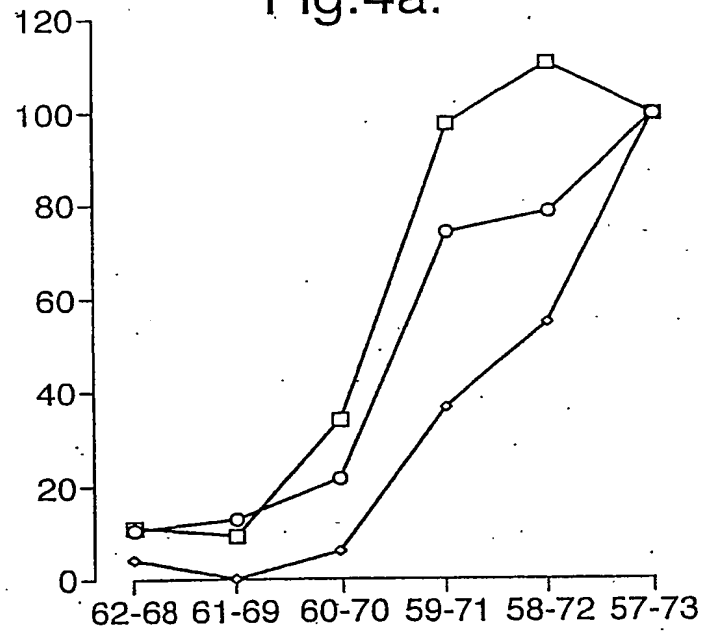
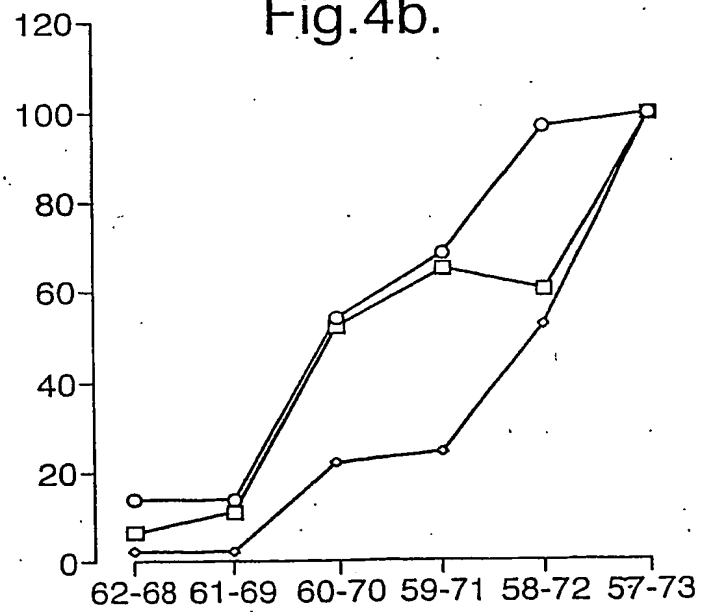


Fig.4b.



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Fig.5.

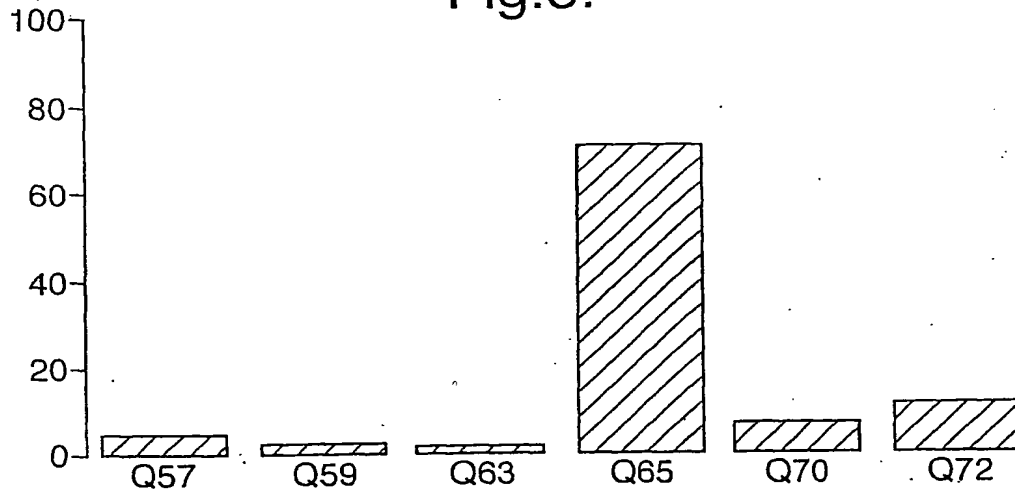
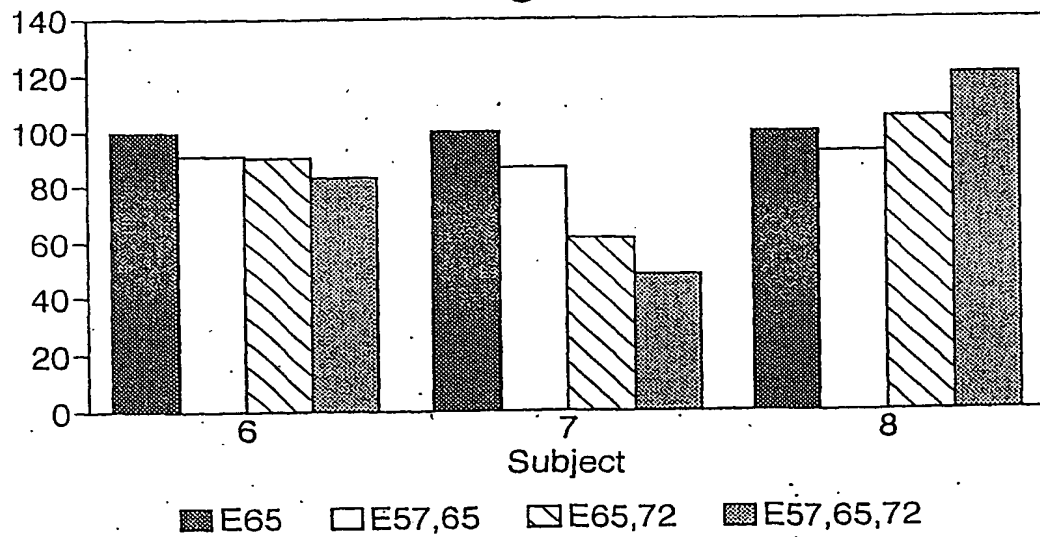


Fig.6.



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Fig.7a.

CD4 depletion

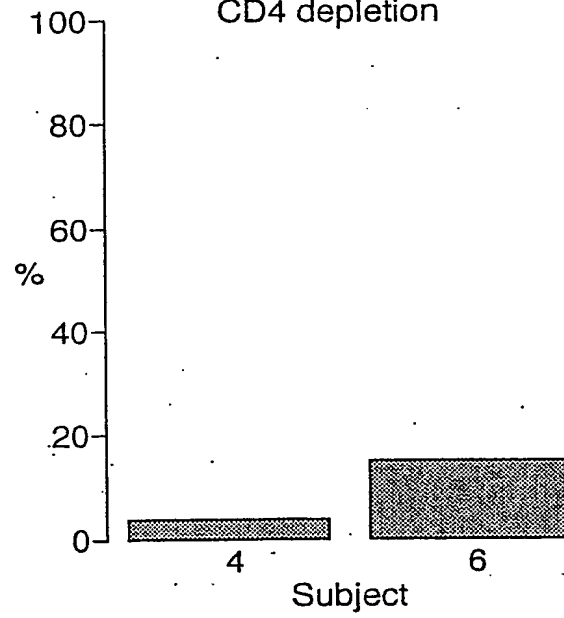
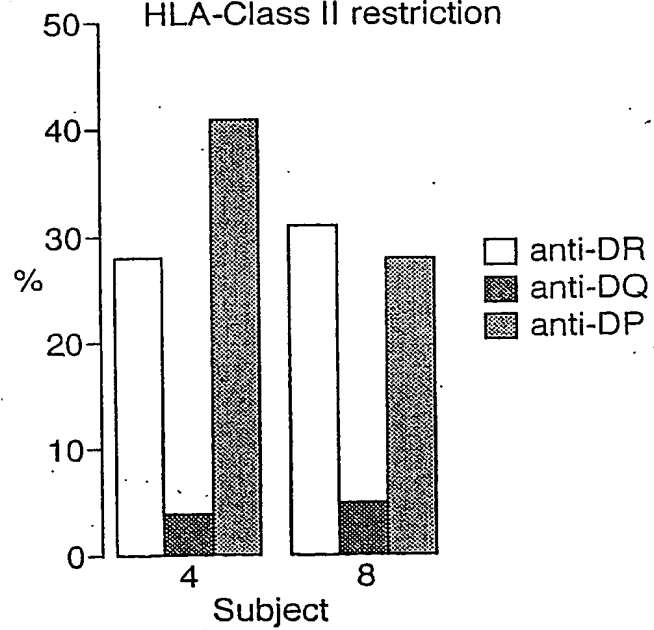
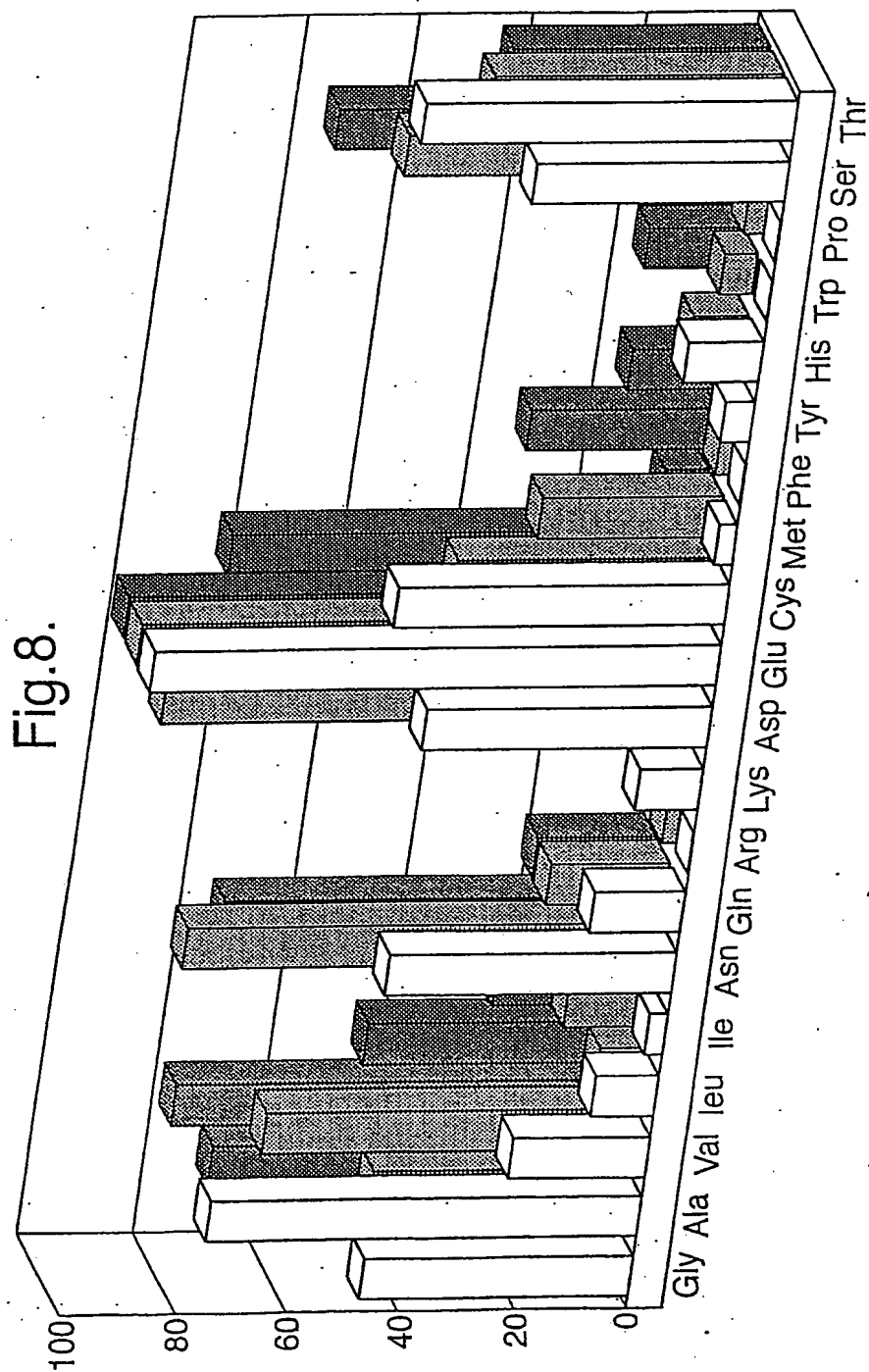


Fig.7b.

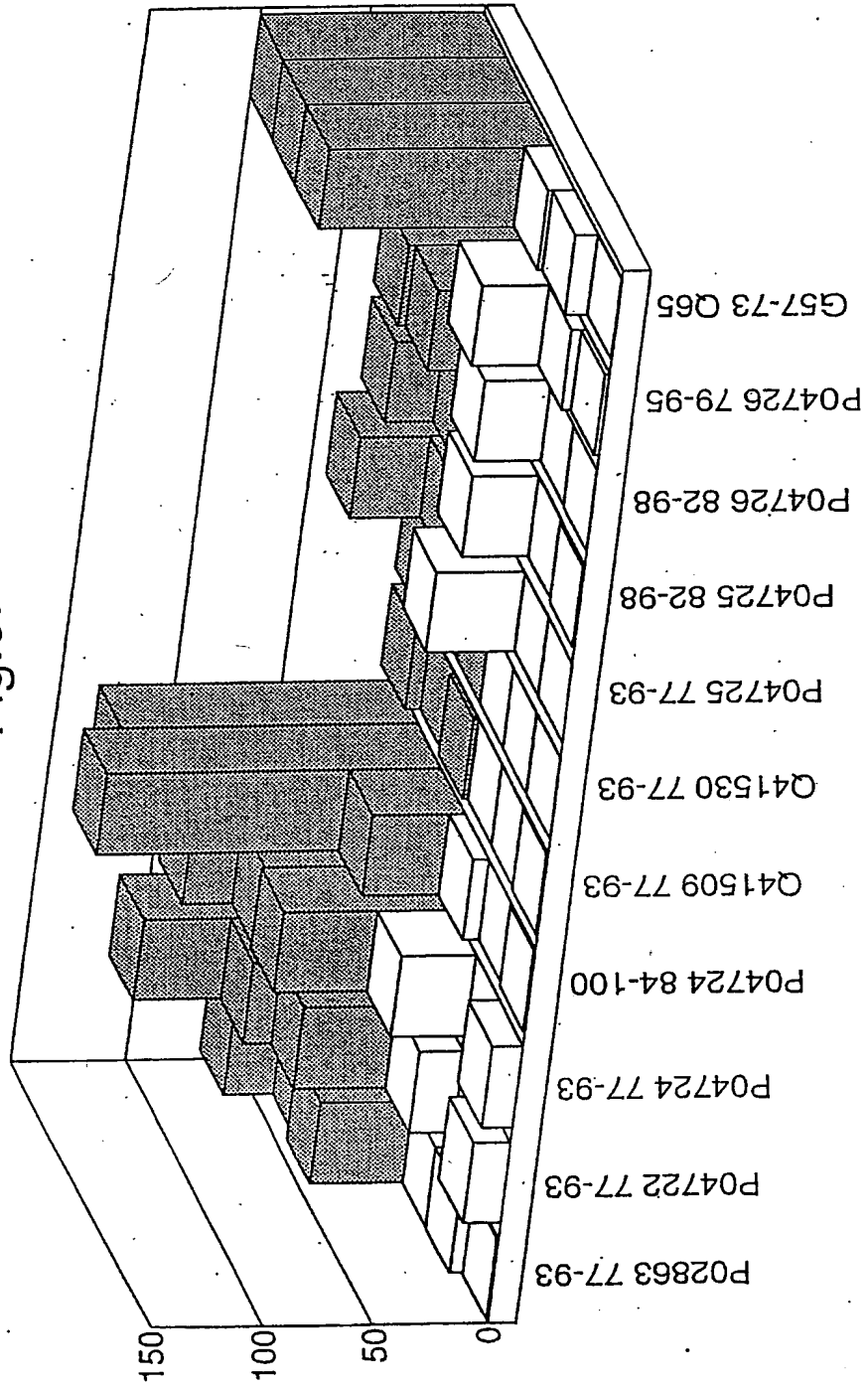
HLA-Class II restriction





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Fig.9.



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Fig.10.

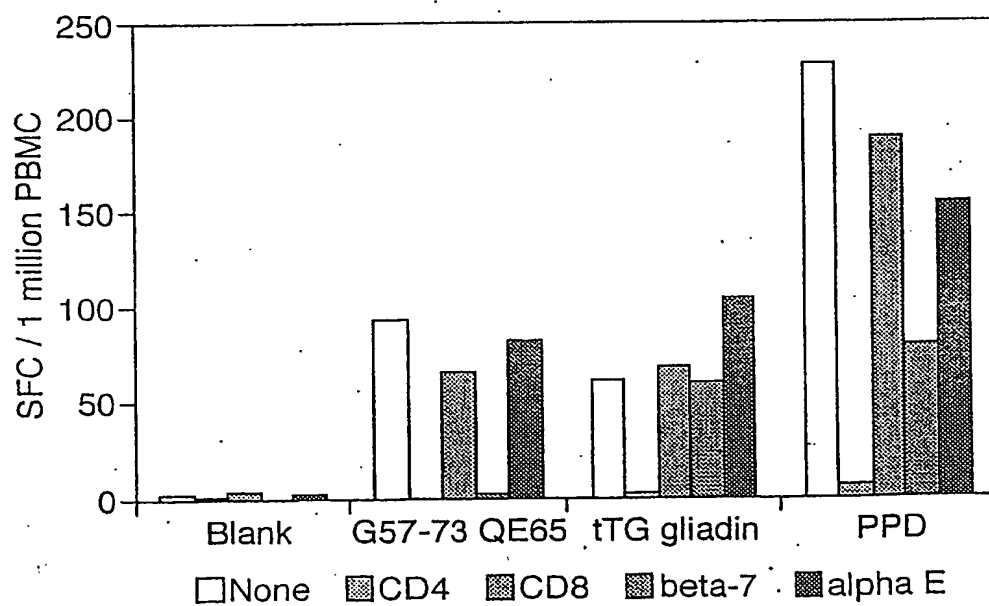
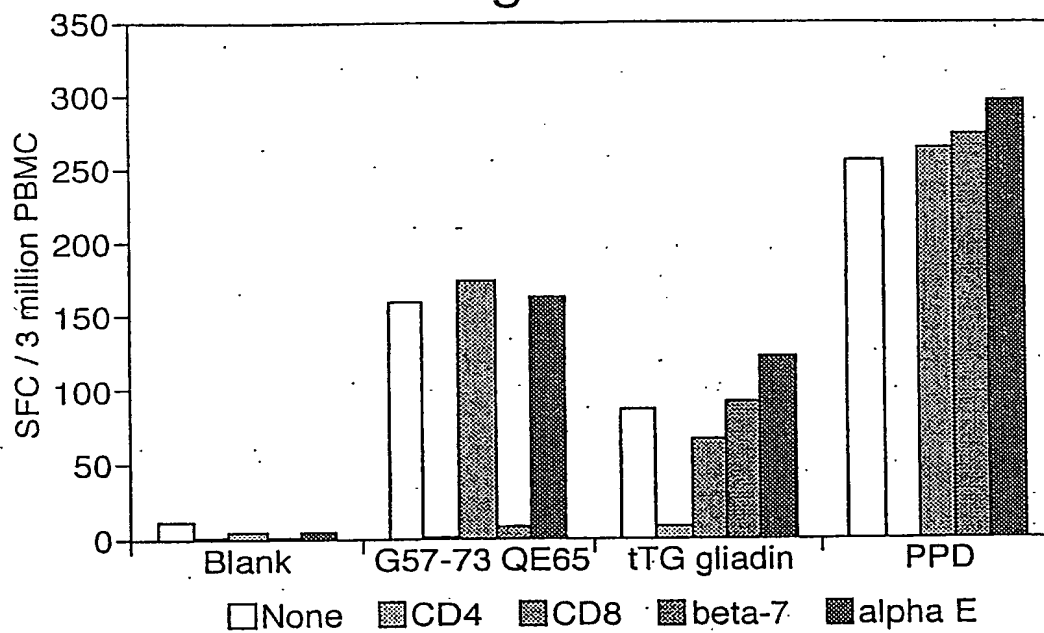


Fig.11.

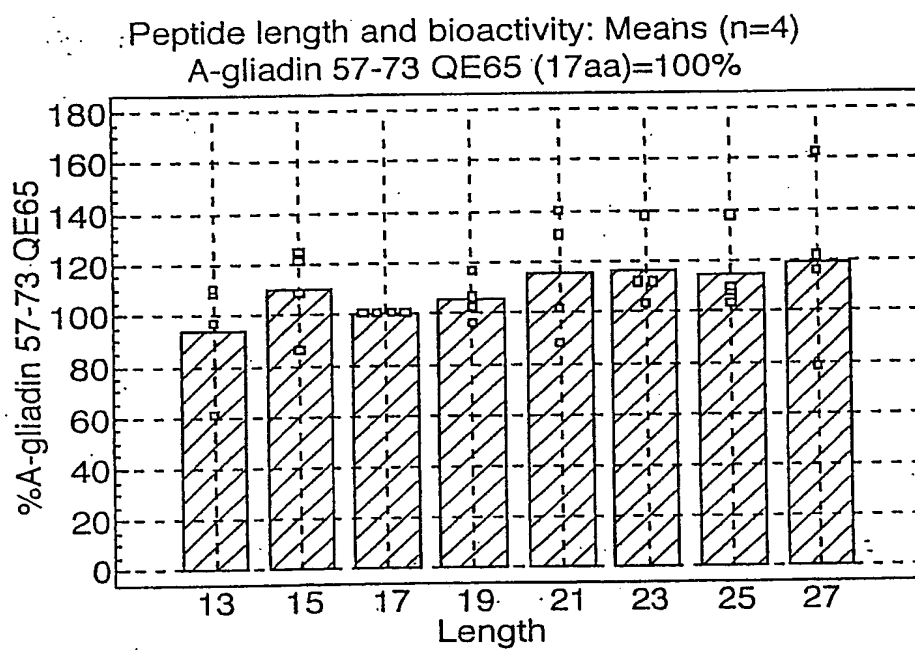


Fig.12a.

Dose response to A-gliadin 57-73 QE65:
QLQFPFQPPELPYPQPQS.

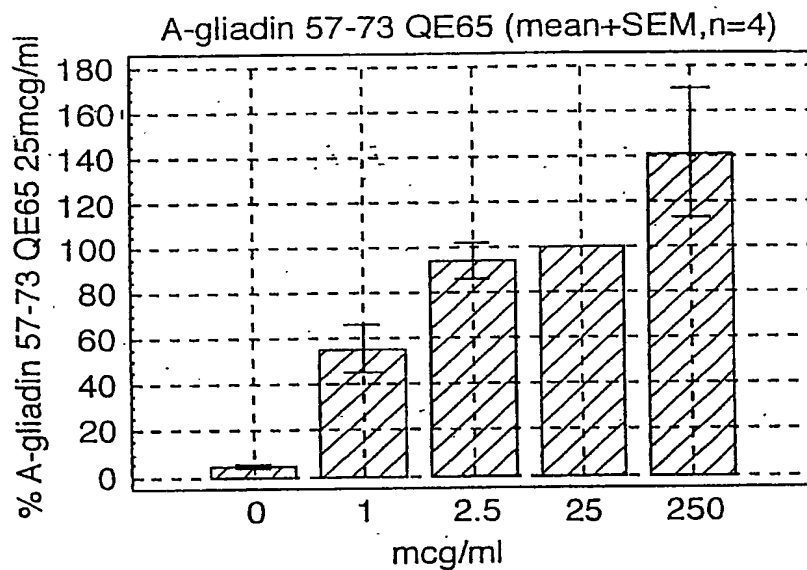


Fig.12b.

Dose response to GDA4_WHEAT P04724 84-100 QE92:
PQLPYPQPPELPYPQPQP.

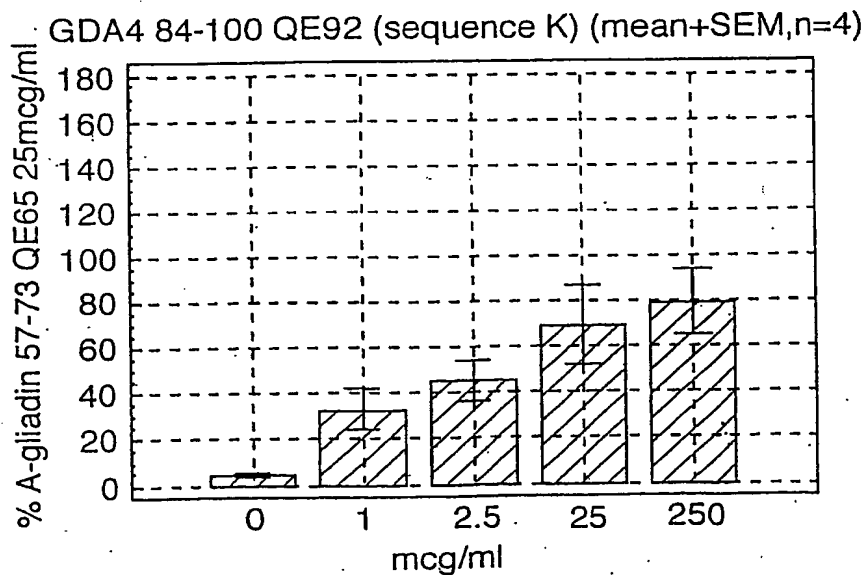


Fig.12c.

Dose response to A-gliadin 57-73:
QLQFPQPQLPYQPQPS (2.5, 25 & 250 mcg/ml),
and A-gliadin 57-73 (25 mcg/ml) + tTG treatment.

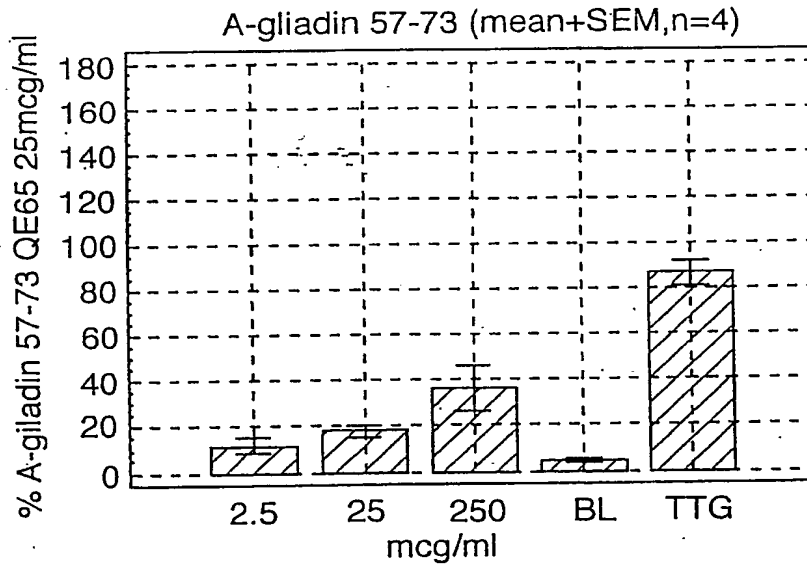


Fig.12d.

Dose response to GDA4_WHEAT P04724 84-100:
PQLPYQPQLPYQPQP (2.5, 25 & 250 mcg/ml),
and P04724 84-100 (25 mcg/ml) + tTG treatment.

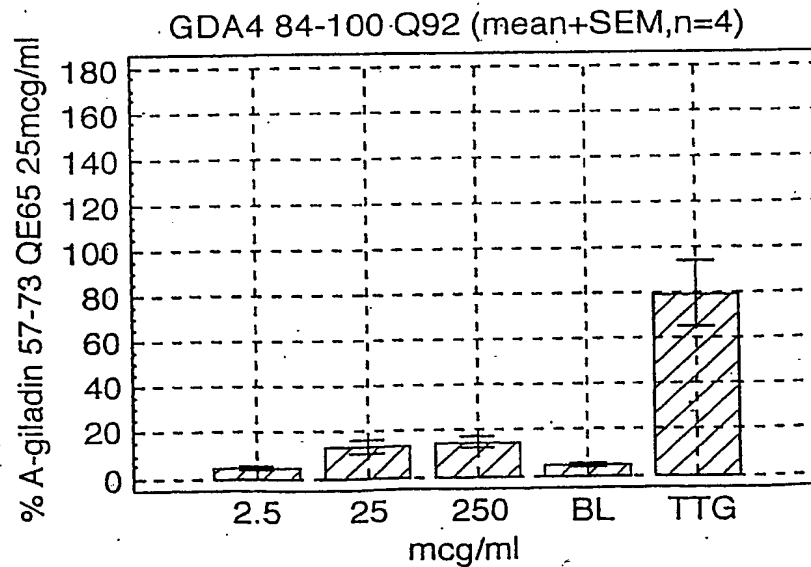


Fig.12e.

Dose response to the DQ2-restricted α gliadin T cell epitope A-gliadin 57-68 QE65: QLQPFPPQPELPY (E65) (2.5, 25 & 250 mcg/ml), and A-gliadin 57-68: QLQPFPPQPQLPY (Q65) (25 mcg/ml) +/- tTG treatment.

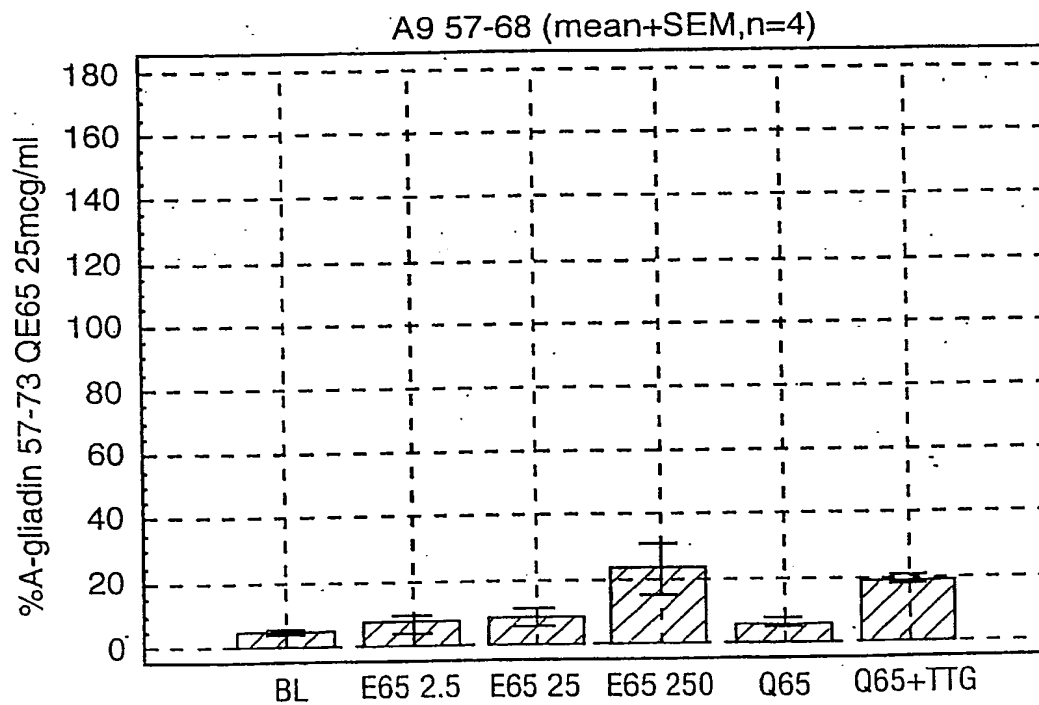


Fig.12f.

Dose response to the DQ2-restricted α gliadin T cell epitope α -2 62-75 QE65 & QE72: PQPELPYPQPELPY (E65) (2.5, 25 & 250 mcg/ml), and α -2 62-75: PQPQLPYPQPQLPY (Q65) (25 mcg/ml) +/- tTG treatment.

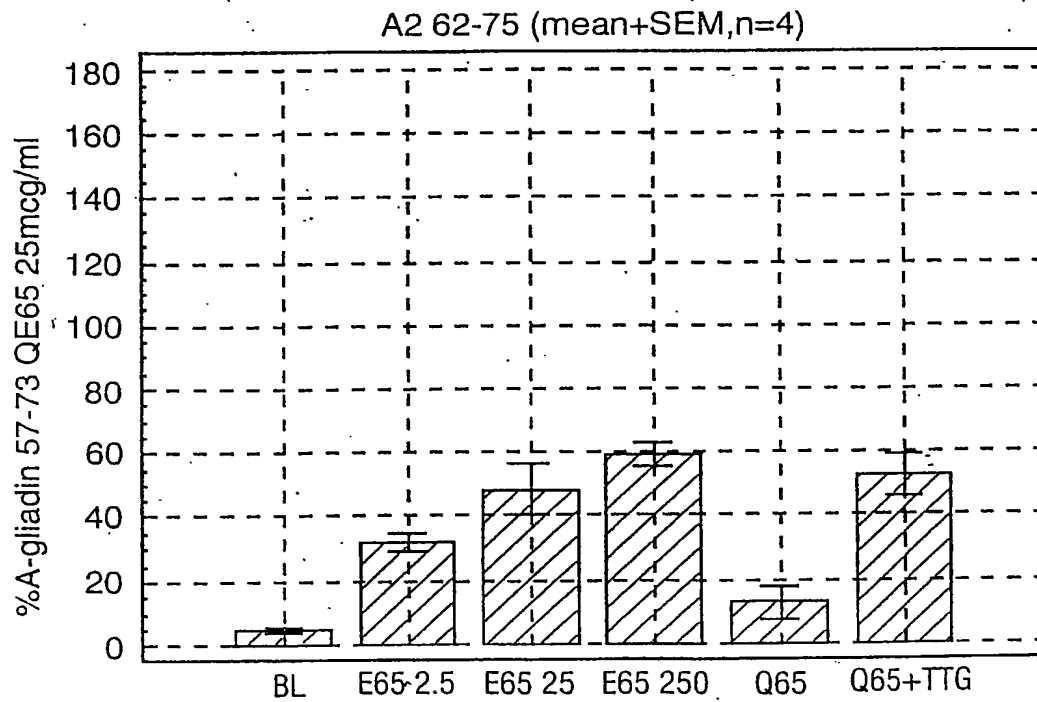


Fig.12g.

Dose response to the DQ8-restricted α gliadin T cell epitope GDA9 202-219: QE208 & 216: QQYPSGEGSFQPSQENPQ (E) (25 & 250 mcg/ml), and to GDA9 202-219 QQYPSGQGSFQPSQQNPQ (Q) (25 mcg/ml) +/- tTG treatment.

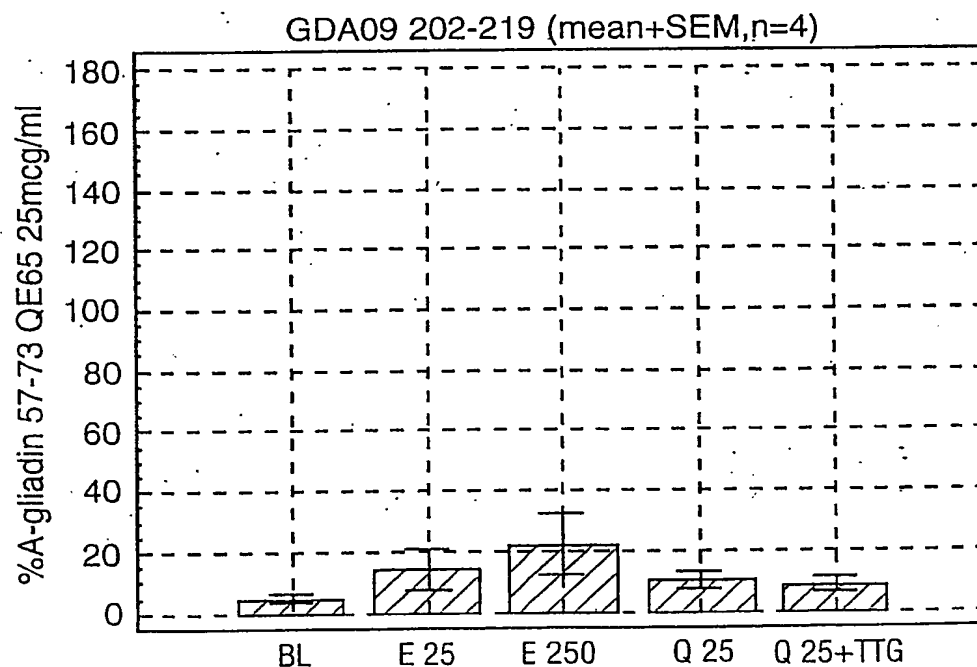


Fig.12h.

Dose response to the DQ2-restricted γ gliadin T cell epitope GDB2 134-153 QE140, 148,150: QQLPQPEQPQQSFPEQERPF (E) (25 & 250 mcg/ml), and to GDB2 134-153: QQLPQPQQPQQSFPPQQRPF (Q) (25 mcg/ml) +/- tTG treatment.

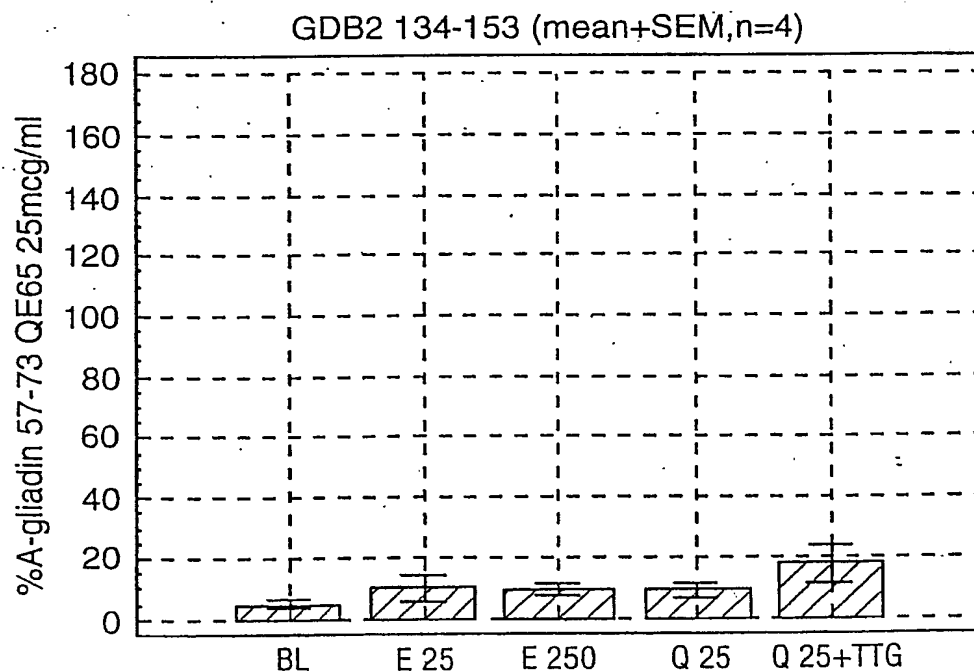


Fig.13a.

Dose response to gliadin digest by
chymotrysin.

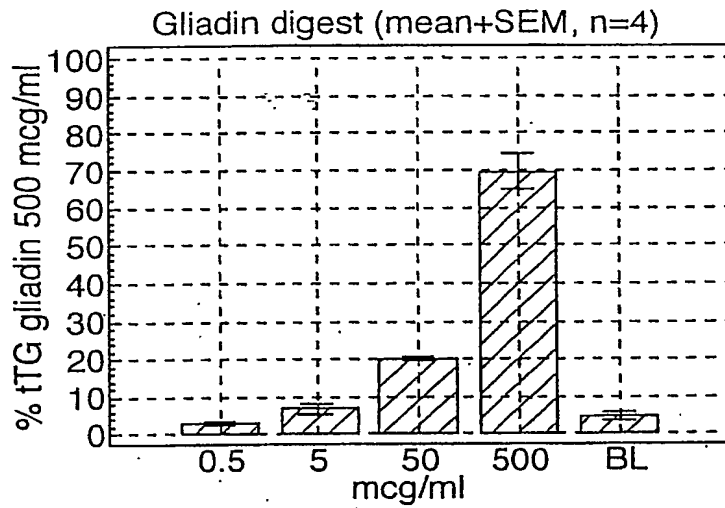


Fig.13b.

Dose response to gliadin digested by
chymotrysin then treated with tTG.

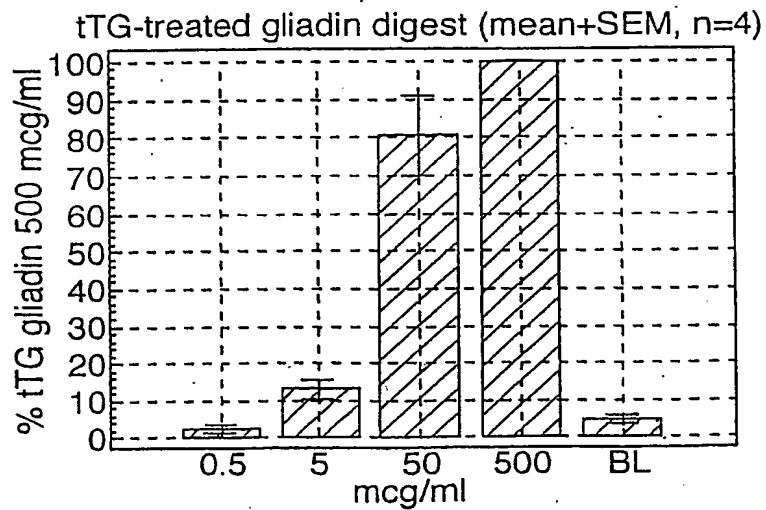
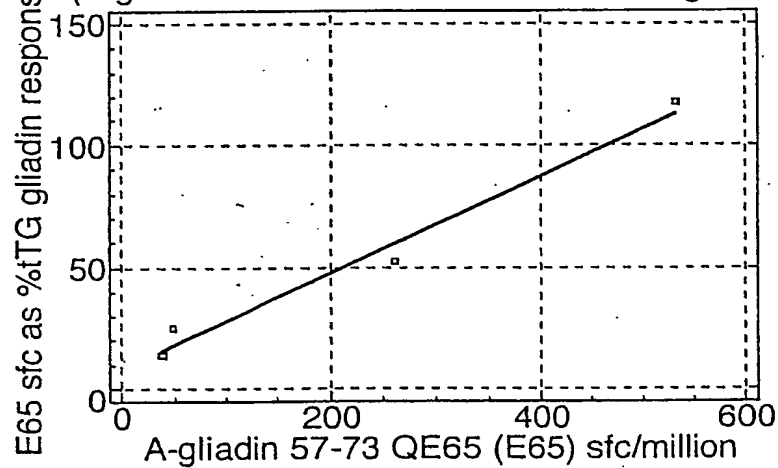


Fig.13c.

Total ELISpot responses to A-gliadin 57-73 QE65 (25mcg/ml) versus A-gliadin 57-73 QE65 responses as percent of tTG gliadin (500mcg/ml) responses.

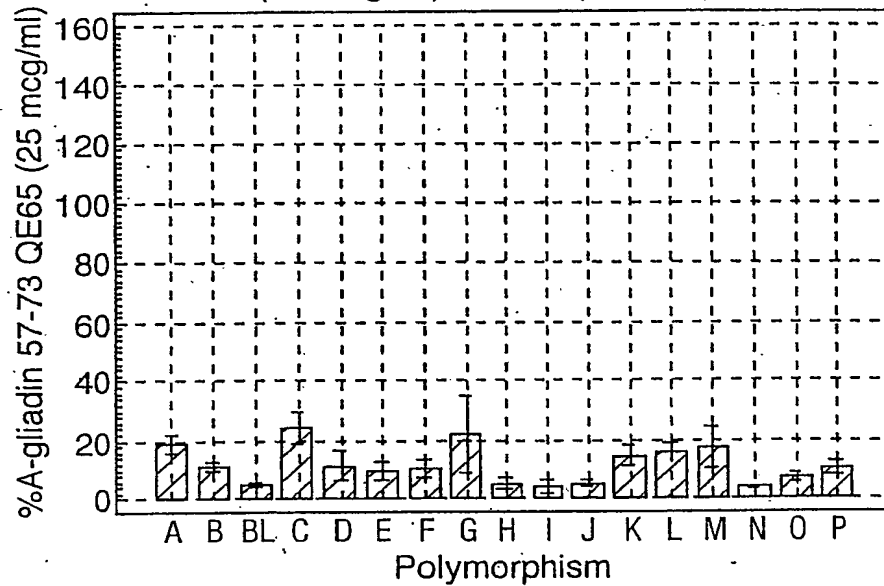
Responses to dominant epitope and complete antigen (A-gliadin 57-73 QE65 and tTG-treated gliadin)



(Fig.14.)

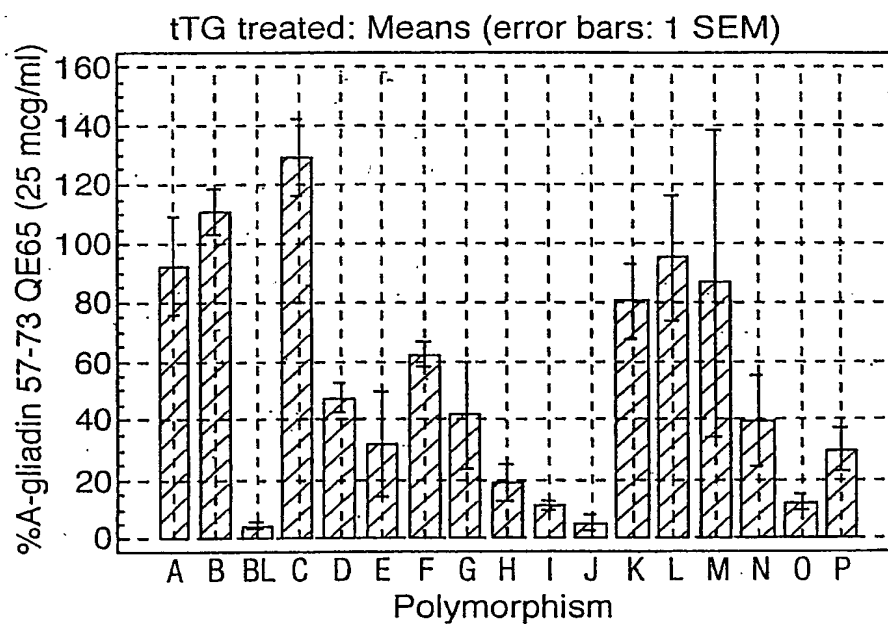
Bioactivity of gliadin polymorphisms of A-gliadin 57-73
(A) in coeliac subjects 6/7 days after gluten challenge
(Gamma-Interferon Elispot) (n=4).

Fig.14a. Unmodified (25 mcg/ml): Means (error bars: 1 SEM)



| | | | |
|---|--------------------|---|--------------------|
| A | QLQPFPPQPQLPYQPQPS | I | QLQPFPPQPQLSYSQPQP |
| B | QLQPFPPQPQLPYQPQP | J | QPQPFPFPQLPYPQTQP |
| C | QLQPFPPQPQLPYQPQL | K | PQLPYQPQLPYQPQP |
| D | QLQPFPPQPQLPYLQPQS | L | PQLPYQPQLPYQPQL |
| E | QLQPFPPRPQLPYQPQP | M | PQPQFPLPQLPYQPQS |
| F | QLQPFPPQPQLPYSQPQP | N | PQPQFPFPQLPYQPQS |
| G | QLQPFLLQPQLPYSQPQP | O | PQPQFPFPQLPYPQTQP |
| H | QLQPFSSQPQLPYSQPQP | P | PQPQFPFPQLPYQPQP |

Fig.14b.

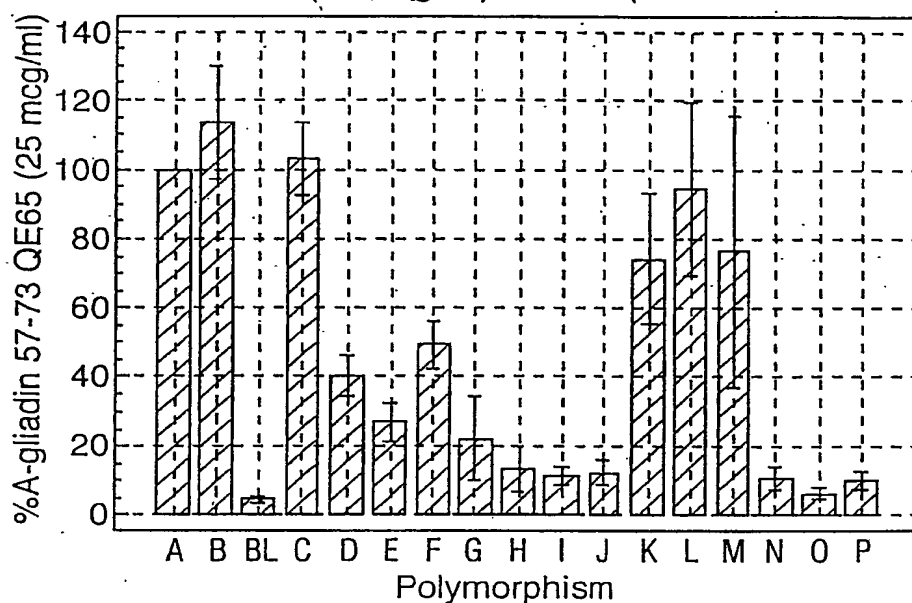


A QLQPFPPQPQLPYQPQSQS
 B QLQPFPPQPQLPYQPQPQ
 C QLQPFPPQPQLPYQPQQL
 D QLQPFPPQPQLPYLQPQS
 E QLQPFPPQPQLPYQPQP
 F QLQPFPPQPQLPYSQPQP
 G QLQPFLLQPQLPYSQPQP
 H QLQPFSSQPQLPYSQPQP

I QLQPFPPQPQLSYSQPQP
 J QPQPFPPQPQLPYPQTQP
 K PQLPYQPQLPYQPQP
 L PQLPYQPQLPYQPQQL
 M PQPQPFLLPQLPYQPQSQS
 N PQPQPFPPQPQLPYQPQSQS
 O PQPQPFPPQPQLPYPQTQP
 P PQPQPFPPQPQLPYQPQP

Fig.14c.

QE65 substituted (25 mcg/ml): Means (error bars: 1 SEM)



| | | | |
|---|-------------------|---|-------------------|
| A | QLQPFPQPQLPYQPQS | I | QLQPFPQPQLSYSQPQP |
| B | QLQPFPQPQLPYQPQP | J | QPQPFPFPQLPYPQTQP |
| C | QLQPFPQPQLPYQPQL | K | PQLPYQPQLPYQPQP |
| D | QLQPFPQPQLPYLQPQS | L | PQLPYQPQLPYQPQL |
| E | QLQPFPQPQLPYQPQP | M | PQPQFPLPQLPYQPQS |
| F | QLQPFPQPQLPYSQPQP | N | PQPQFPPQLPYQPQS |
| G | QLQPFLQPQLPYSQPQP | O | PQPQFPPQLPYPQTQP |
| H | QLQPFLQPQLPYSQPQP | P | PQPQFPPQLPYQPQP |

Fig. 14d. QE65-substituted (2.5 mcg/ml): Means (error bars: 1 SEM)

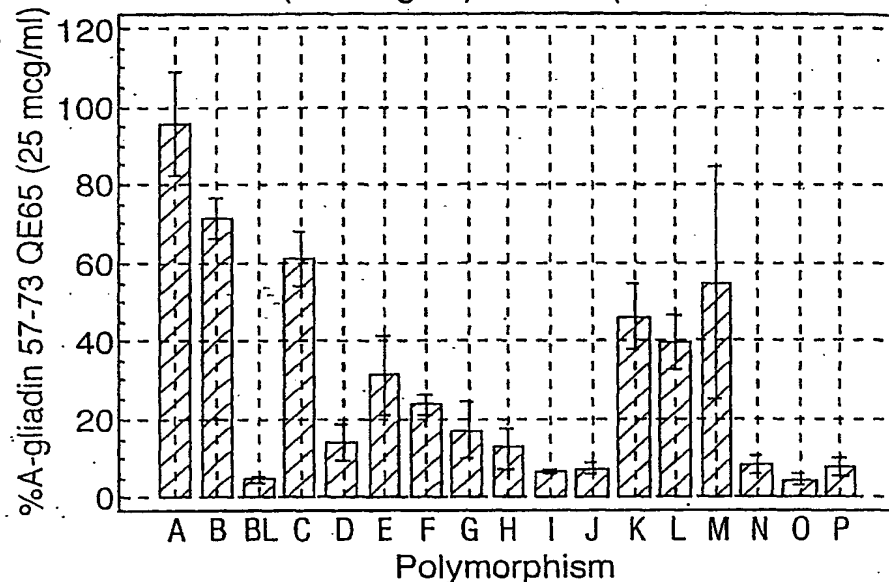
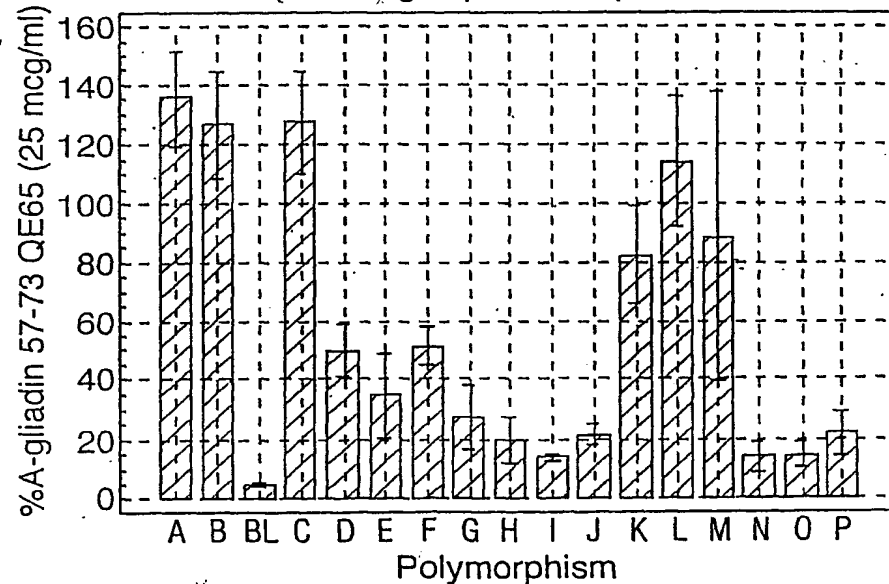


Fig. 14e. QE65-substituted (250 mcg/ml): Means (error bars: 1 SEM)



A QLQPFPPQQLPYQPQS
 B QLQPFPPQQLPYQPQP
 C QLQPFPPQQLPYQPQL
 D QLQPFPPQQLPYLQPQS
 E QLQPFPPQQLPYQPQP
 F QLQPFPPQQLPYSQPQP
 G QLQPFLLQQLPYSQPQP
 H QLQPFSSQQLPYSQPQP

I QLQPFPPQQLSYSQPQP
 J QPQPFPPQQLPYPQTQP
 K PQLPYQPQLPYQPQP
 L PQLPYQPQLPYQPQL
 M PQQQFLLPQLPYQPQS
 N PQQQFPPQQLPYQPQS
 O PQQQFPPQQLPYPQTQP
 P PQQQFPPQQLPYQPQP

Fig.15.

Alanine scan: Means (error bars: 95% CI for mean)

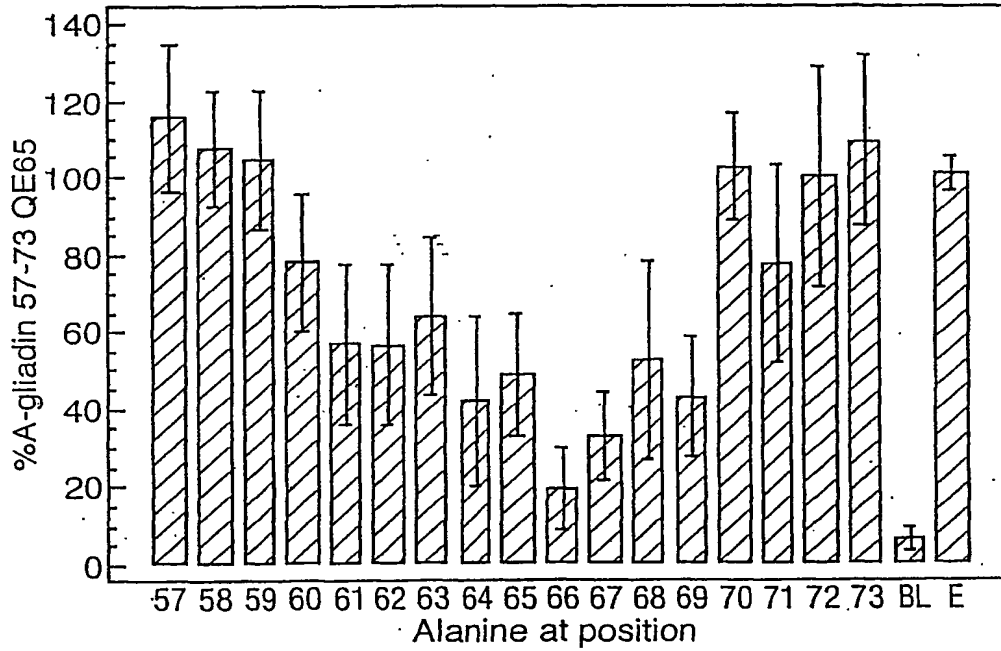


Fig.16.

Lysine scan: Means (error bars: 95% CI for mean)

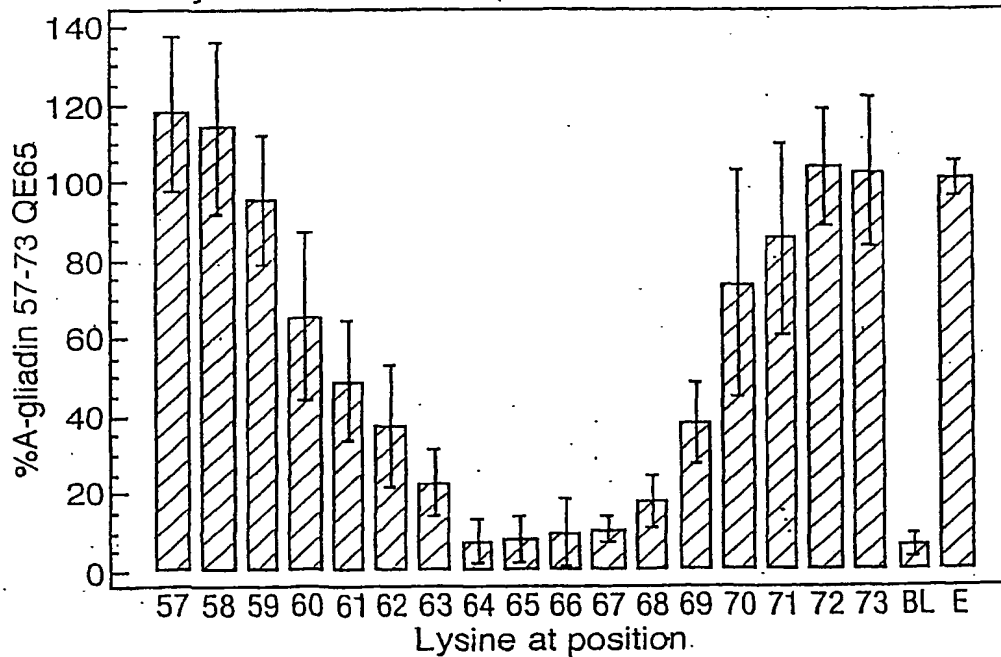


Fig.17.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPF⁶⁰FPQPELPYPQPQS

60.....70

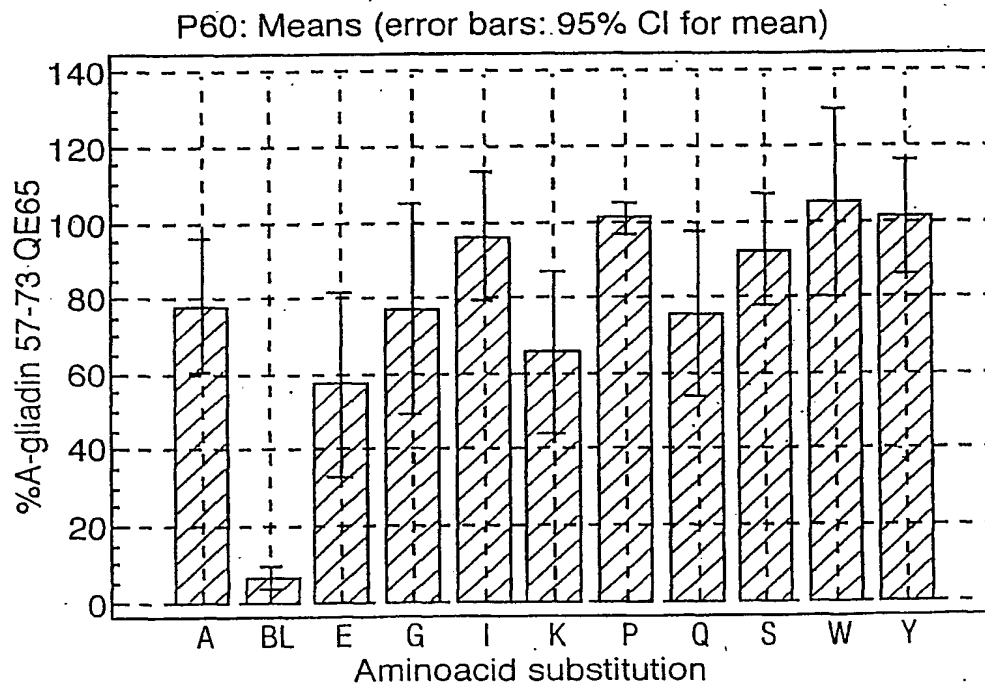
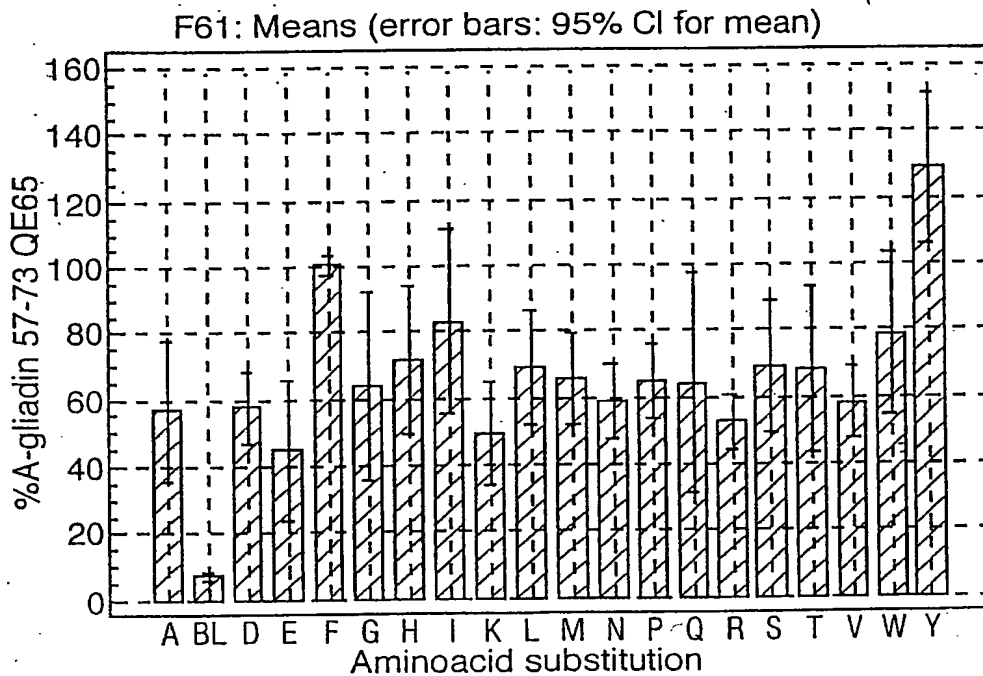


Fig. 18.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPPQPELPYPQPQS

60.....70



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Fig.19.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPPQPELPYPQPQS

60.....70

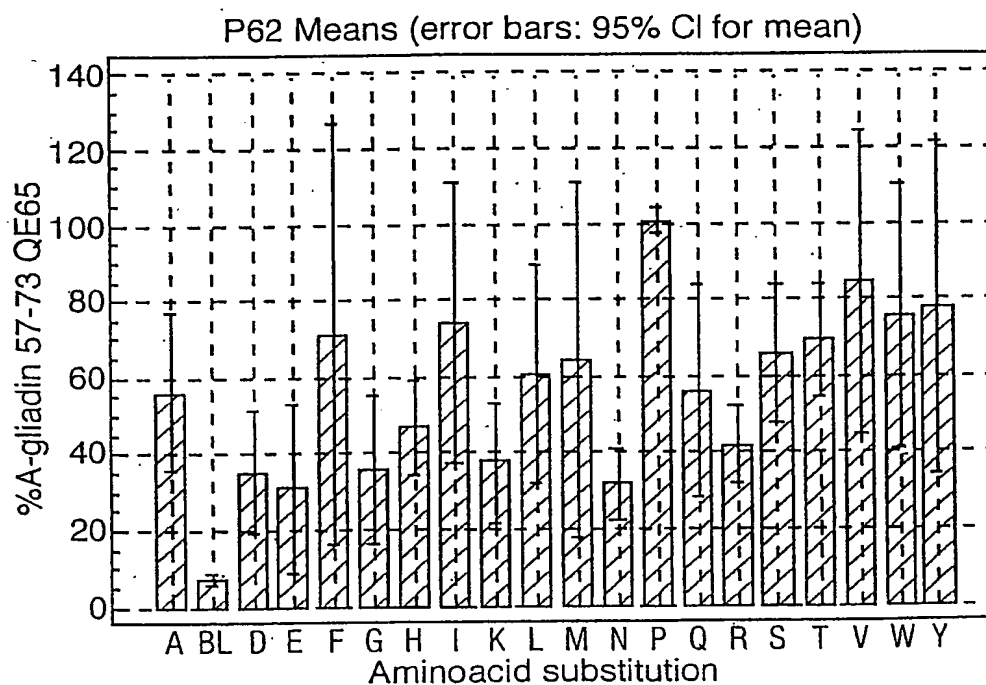


Fig.20.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPPQPELPYPQPQS

60.....70

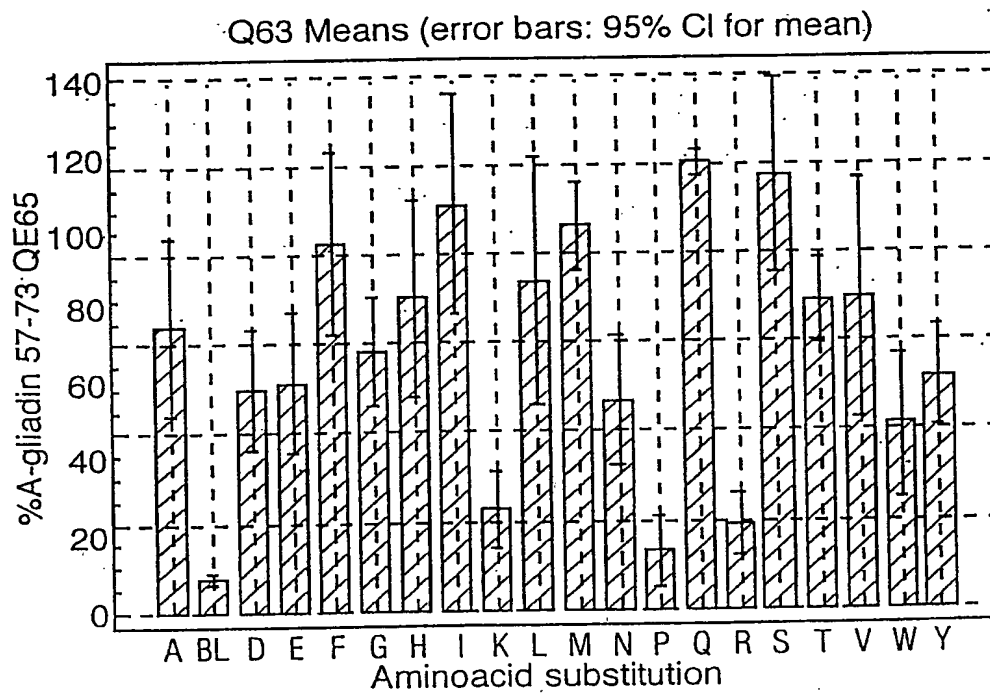


Fig.21.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPPQPELPYPQPQS

60.....70

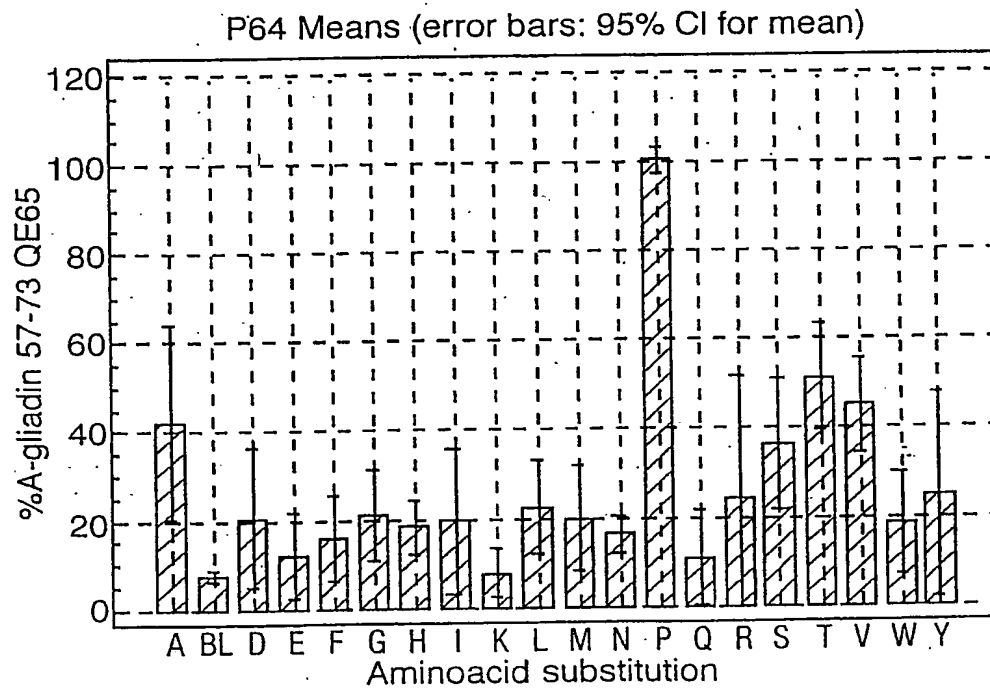


Fig.22.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPF⁶⁰FPQPELPYPQPQS
60.....70

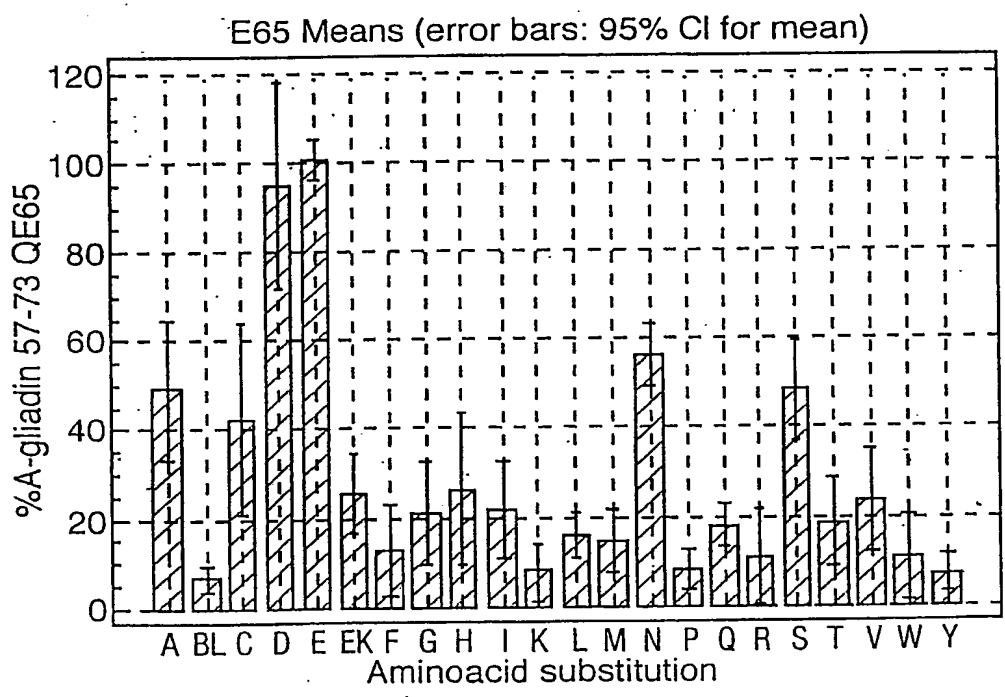


Fig.23.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPPQPELPYPQPQS

60.....70

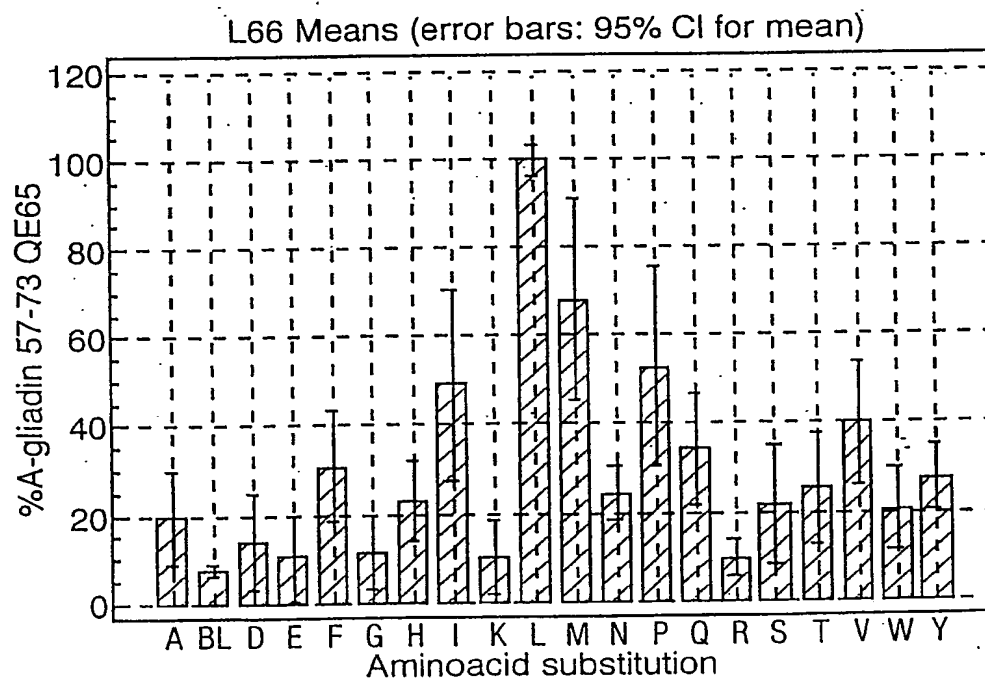


Fig.24.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPPQPELPYPQPQS

60.....70

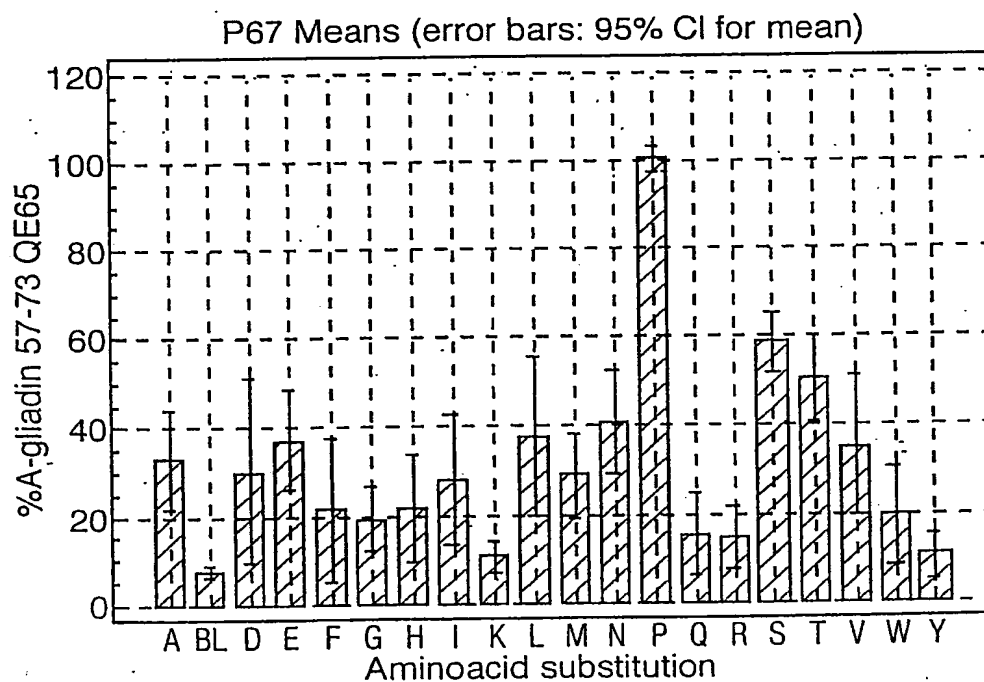


Fig.25.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPPQPELPYPQPQS

60.....70

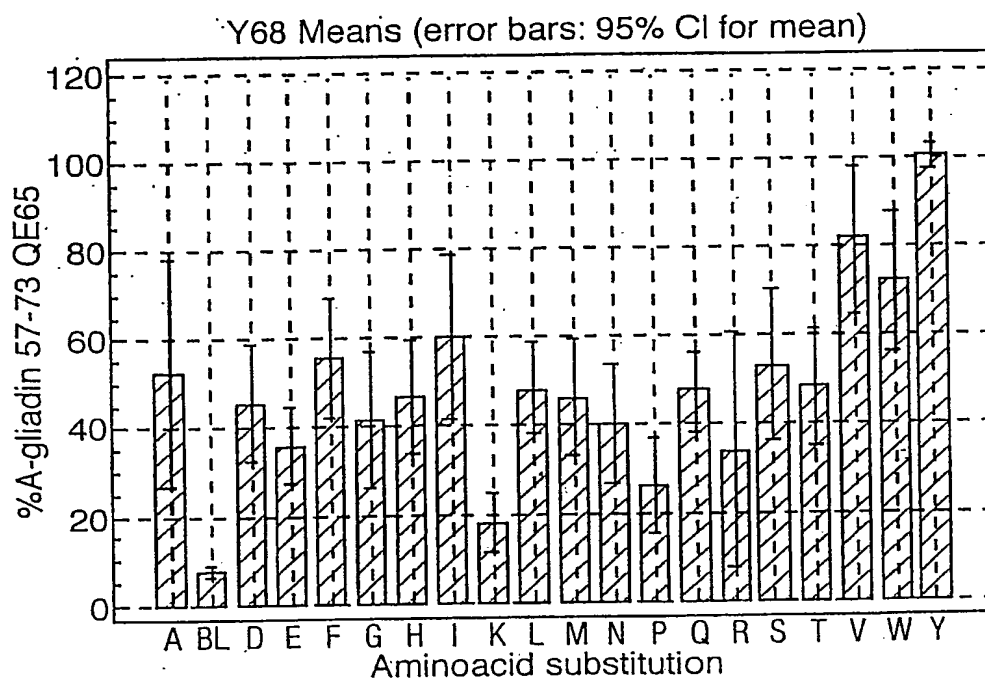


Fig.26.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPFPPQPELPYPQPQS

60.....70

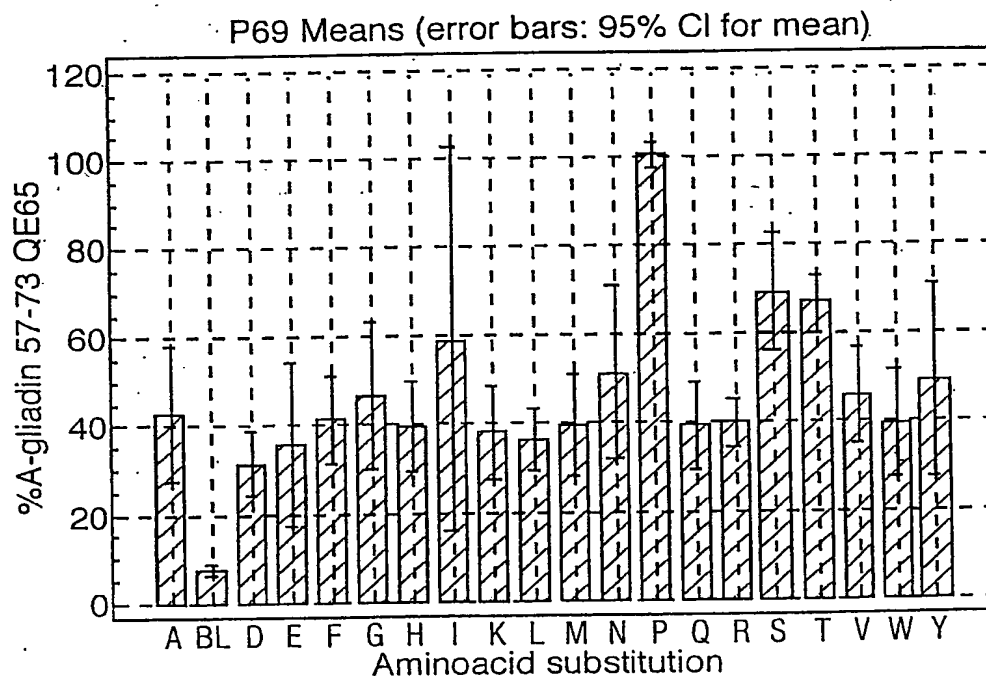
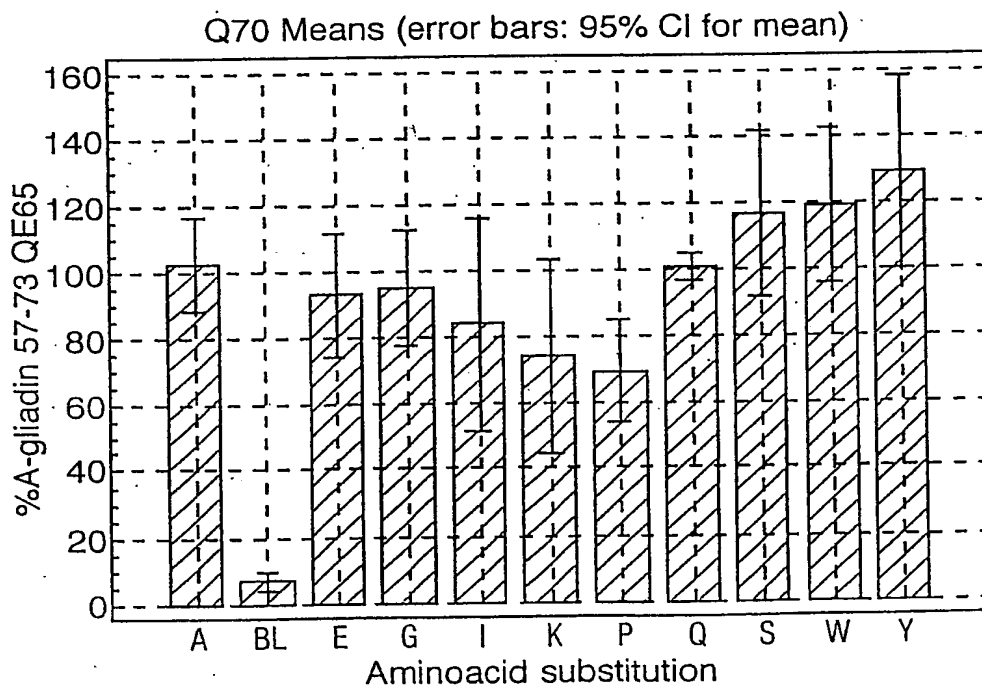


Fig.27.

Agonist activity of A-gliadin 57-73 QE65 variants according to position substituted (Mean of 8 coeliac subjects' PBMC responses in interferon gamma ELISPOT after gluten challenge)

QLQPF⁶⁰PQPELPYPQPQS

60.....70



(Fig.28.)

Interferon gamma ELISpot responses in newly diagnosed and treated coeliac subjects, before and after gluten challenge.

Fig.28a. Untreated, newly diagnosed coeliacs (Mean+SEM, n=9)

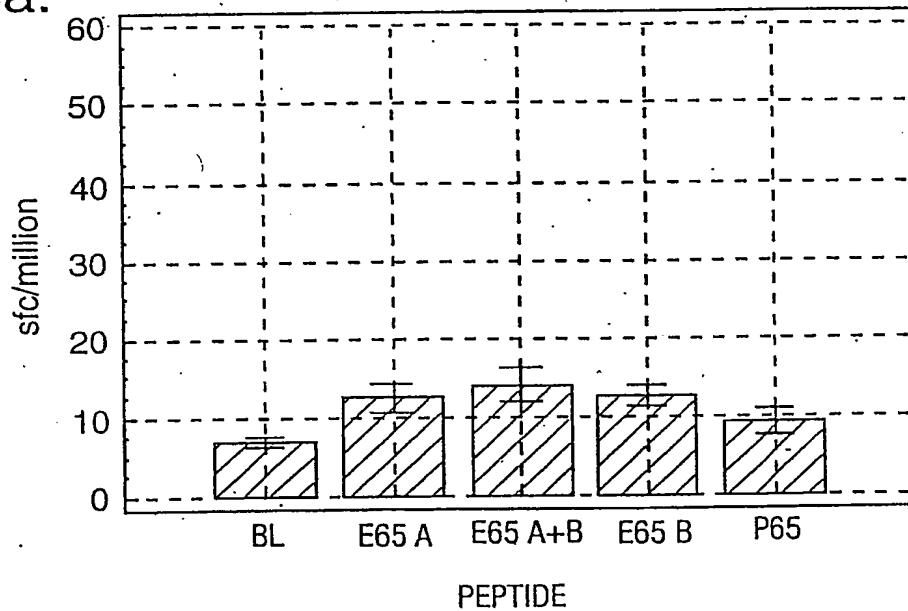


Fig.28b.

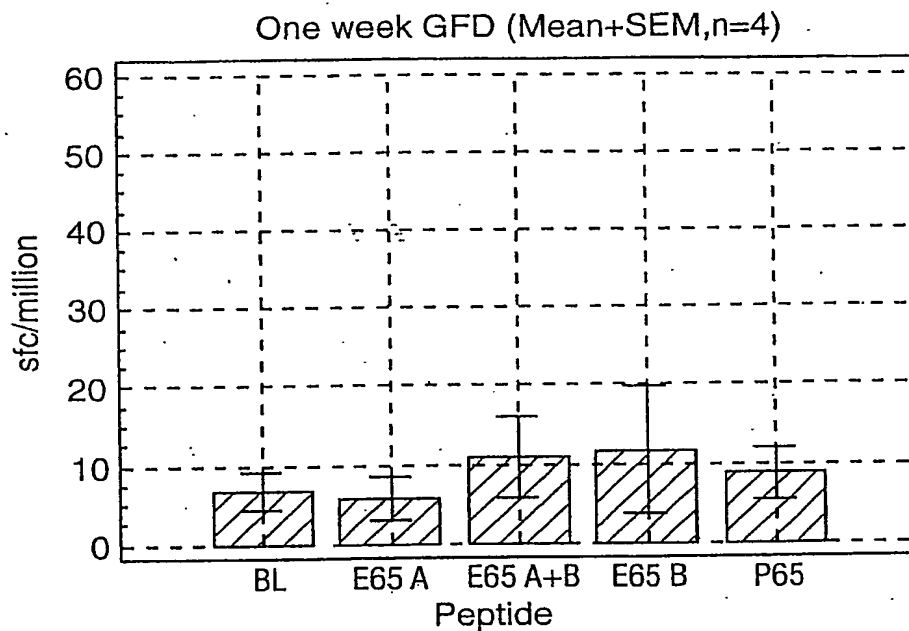


Fig.28c.

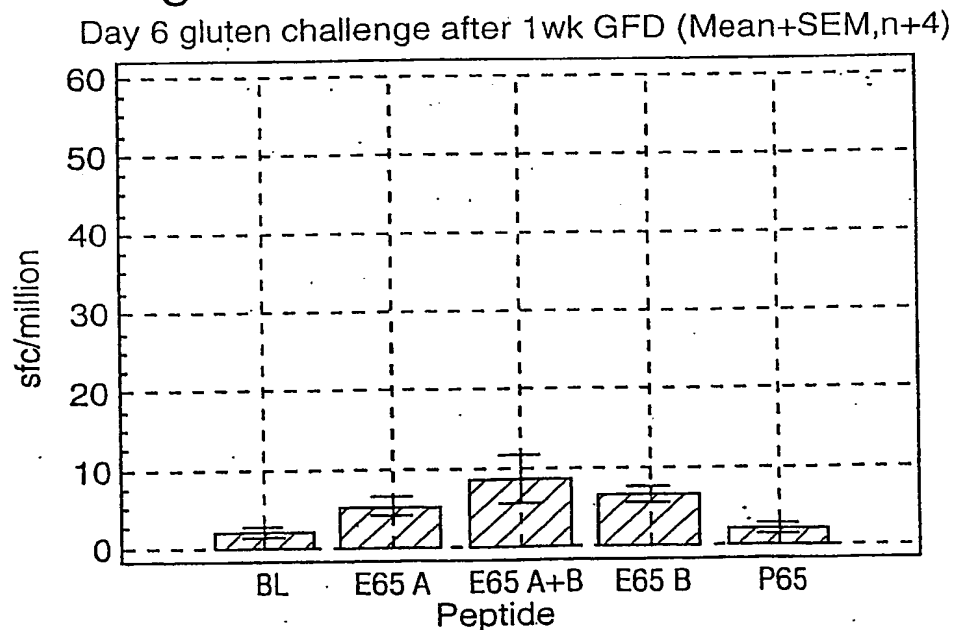


Fig.28d.

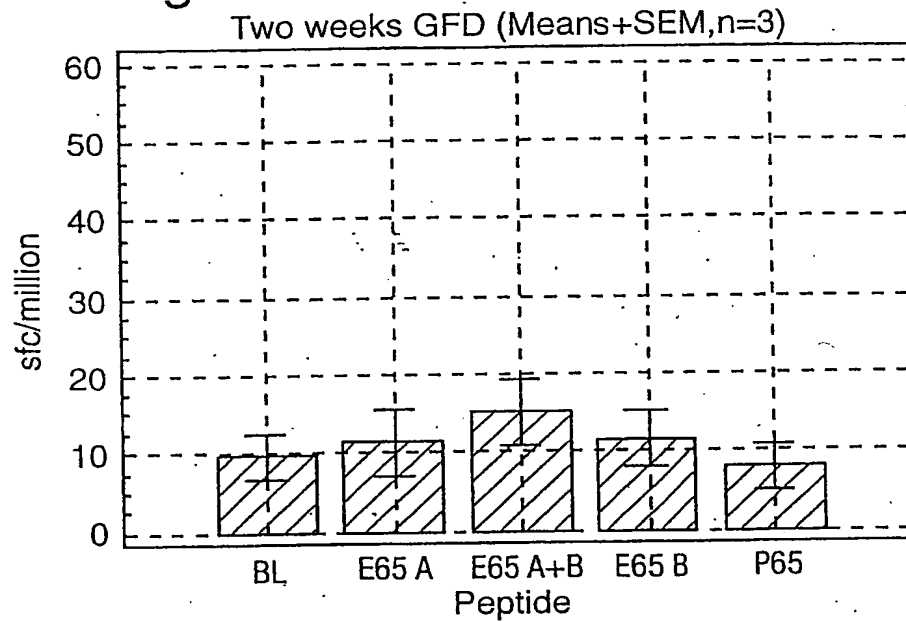


Fig.28e.

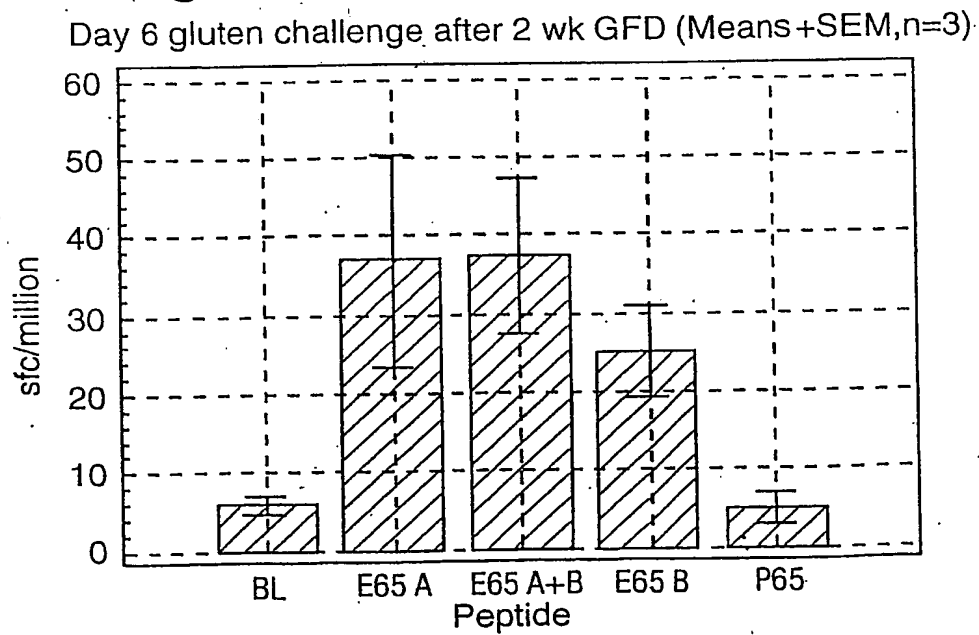


Fig.28f.

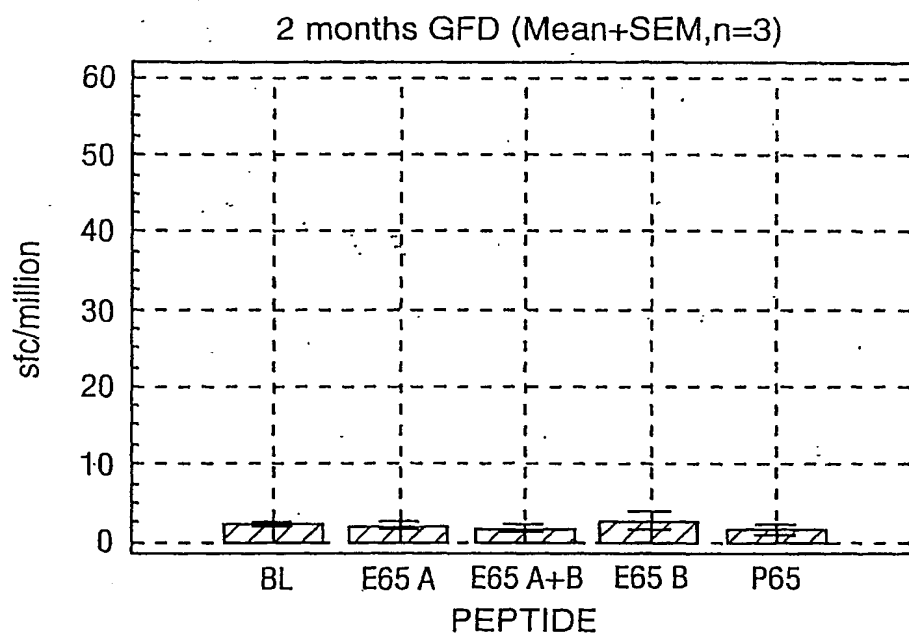


Fig.28g.

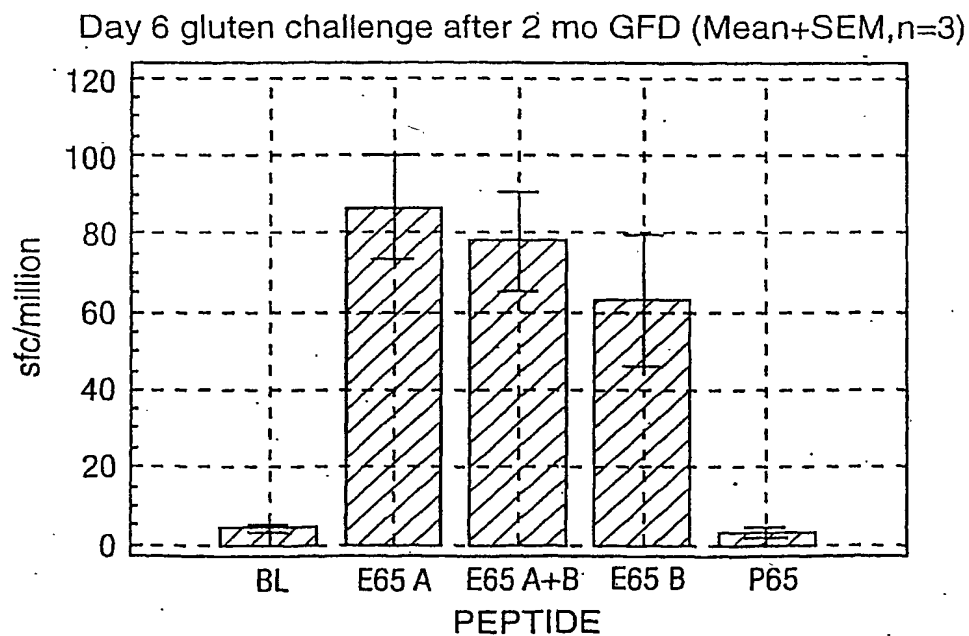
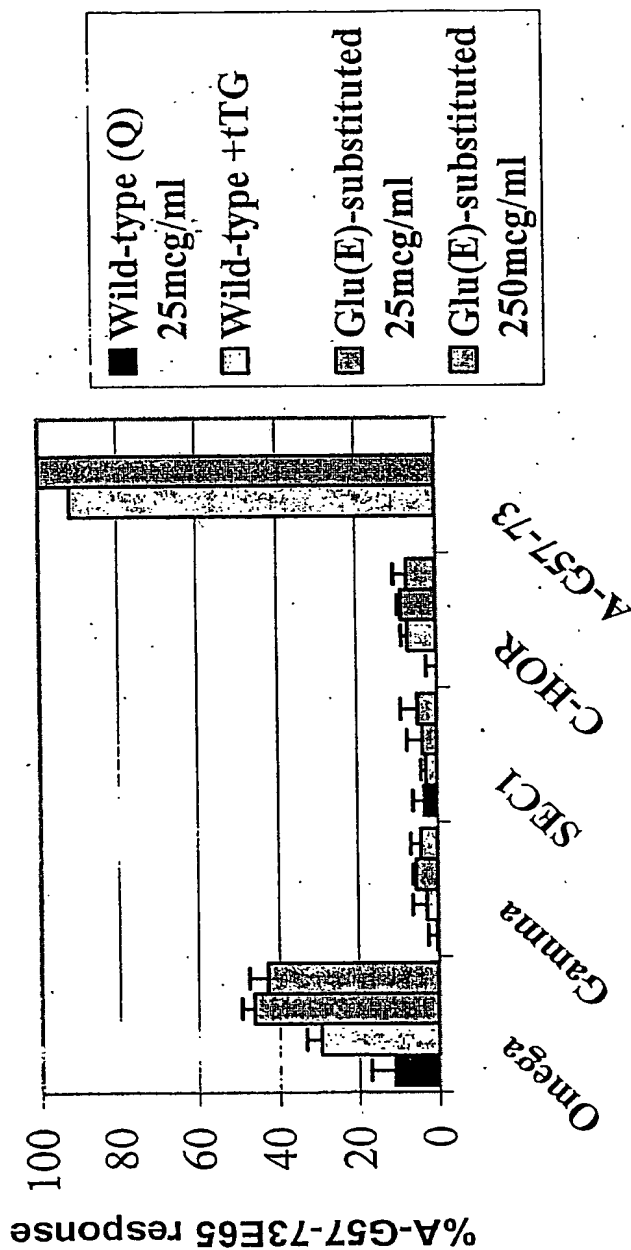


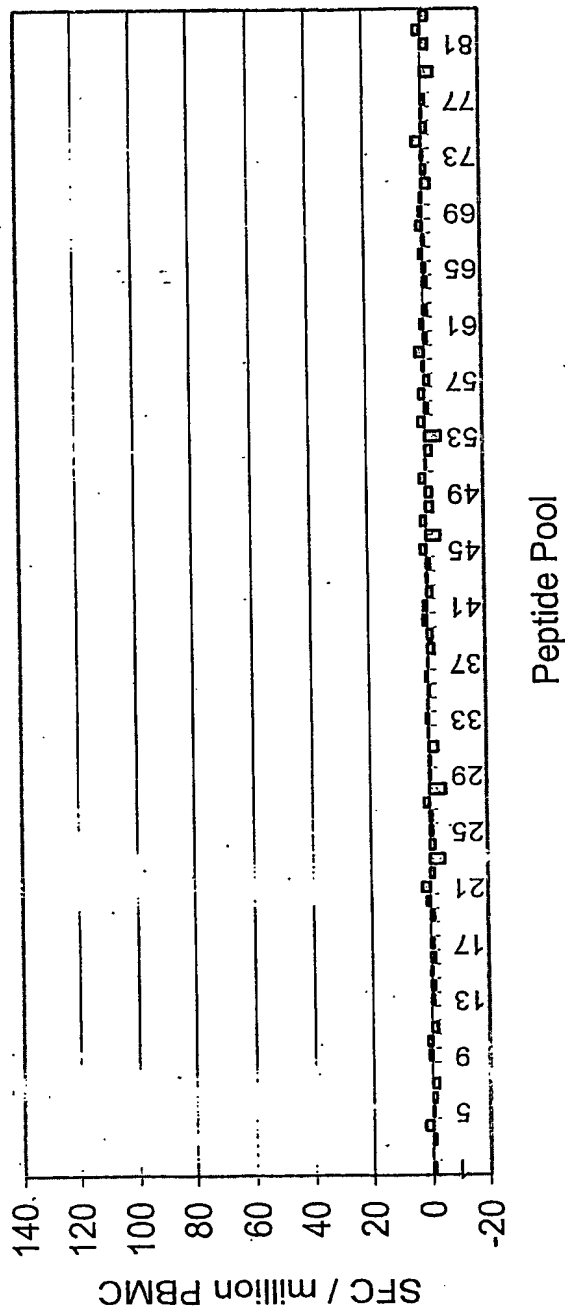
Figure 29. Bioactivity of prolamin homologues of A-gliadin 57-73 (IFNg-ELISpot, mean+SEM, n=6)



Omega: AAG17702 (141-157), Gamma: P21292 (96-112), SEC1: Q43639 (335-351), C-HOR: Q40055 (166-182). E-substituted peptides were synthesized with E for Q at position 9.

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Figure 30. Healthy HLA-DQ2 Subjects: Change in IFNgamma ELISpot Responses to tTG-deamidated Gliadin Peptide Pools (median change Day 6 vs Day 0, n=10)



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Figure 31. Coeliac HLA-DQ2 Subjects: Change in IFNgamma ELISpot
Responses to tTG-deamidated Gliadin Peptide Pools
(median change Day 6 vs Day 0, n=6)

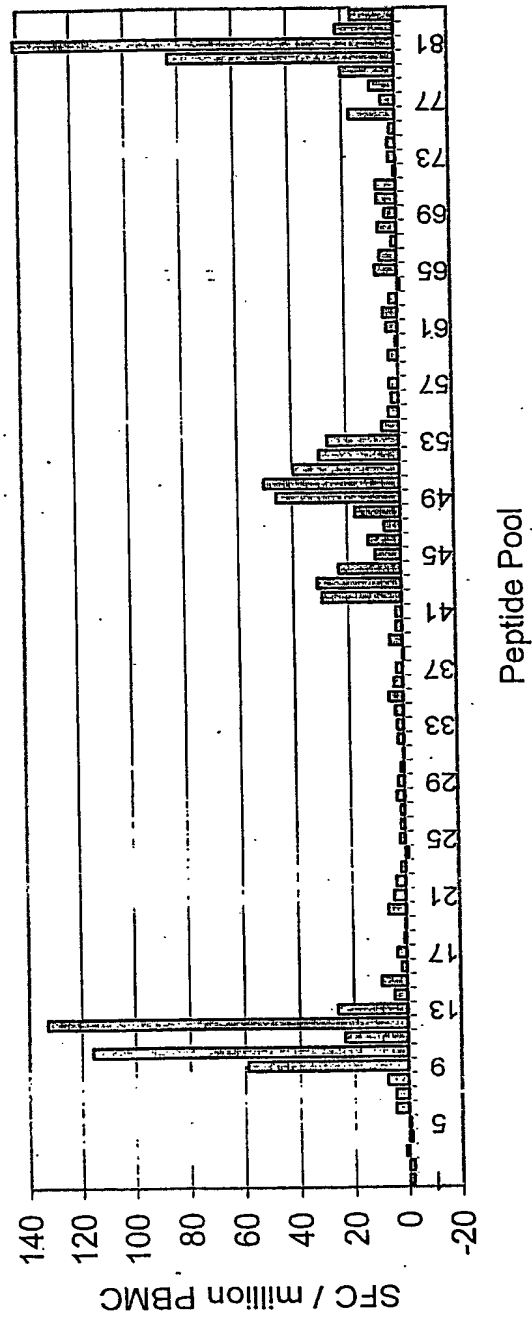


Figure 32. Individual Peptide Contributions to "Summed"
Gliadin Peptide Response

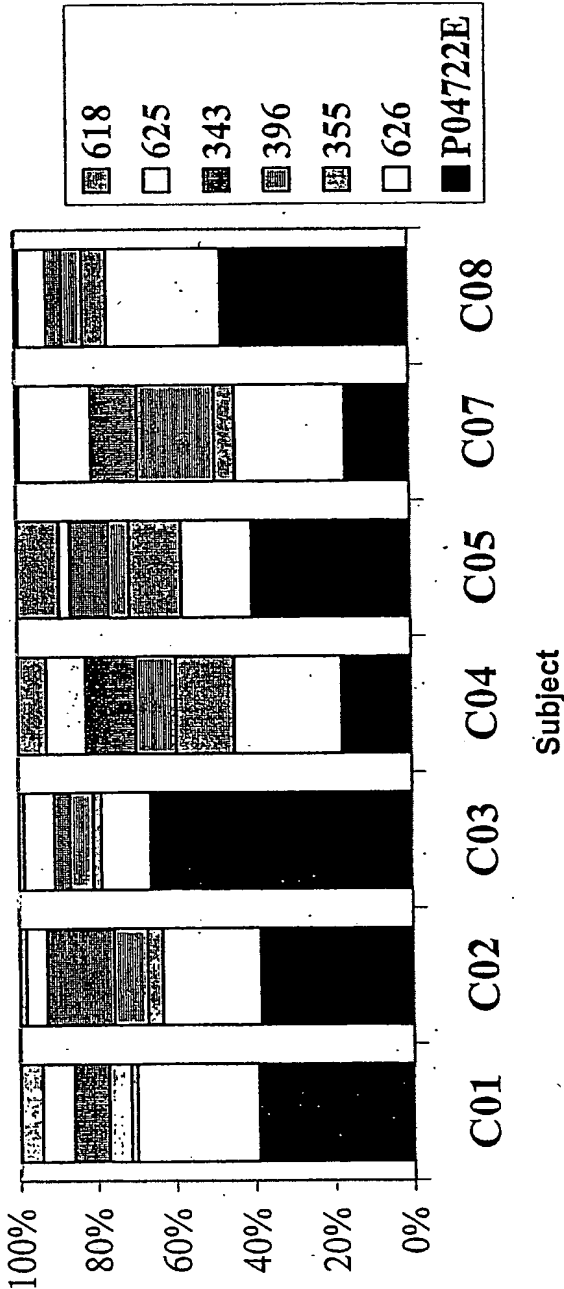
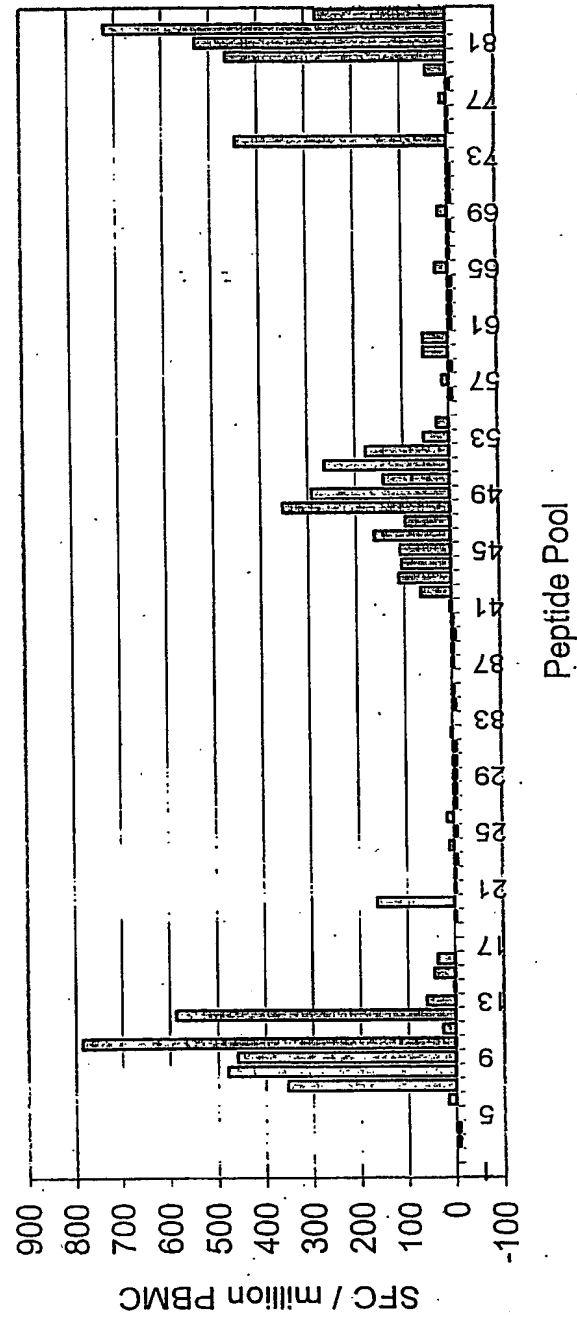


Figure 33. Coeliac HLA-DQ2/8 Subject C08: Gluten challenge induced IFNgamma ELISpot Responses to tTG-deamidated Gliadin Peptide Pools



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Figure 34. Coeliac HLA-DQ2/8 Subject C07: Change in IFNgamma ELISpot Responses to tTG-deamidated Gliadin Peptide Pools

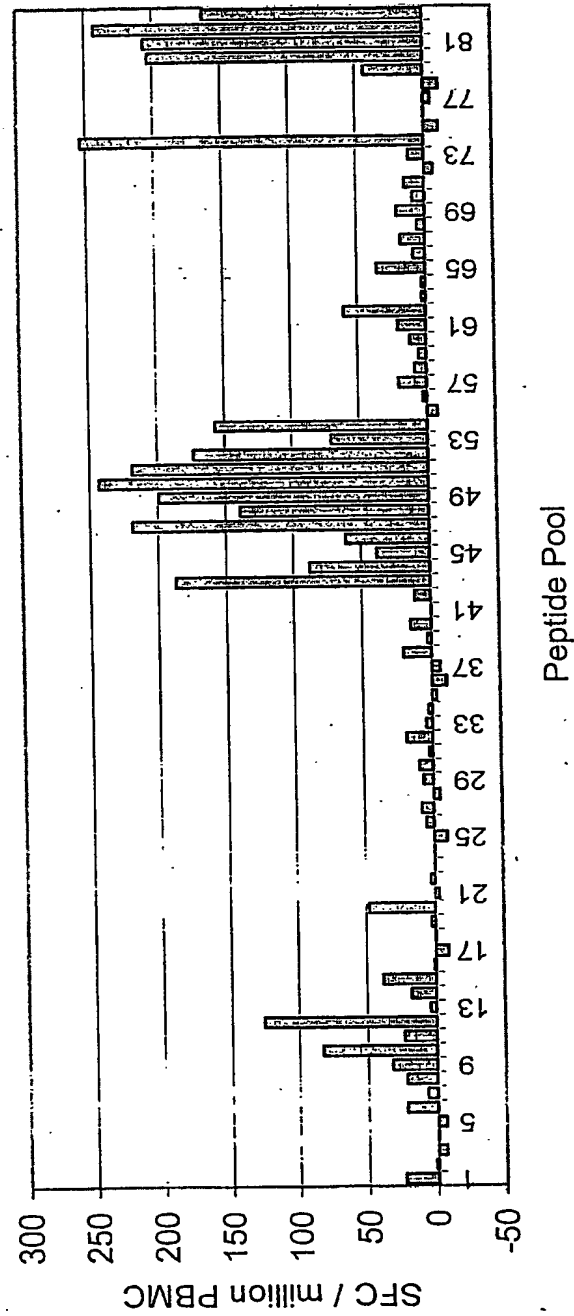


Figure 35. Coeliac HLA-DQ8/7 Subject C12: Gluten challenge induced IFN-gamma ELISpot Responses to tTG-deamidated Gliadin Peptide Pools

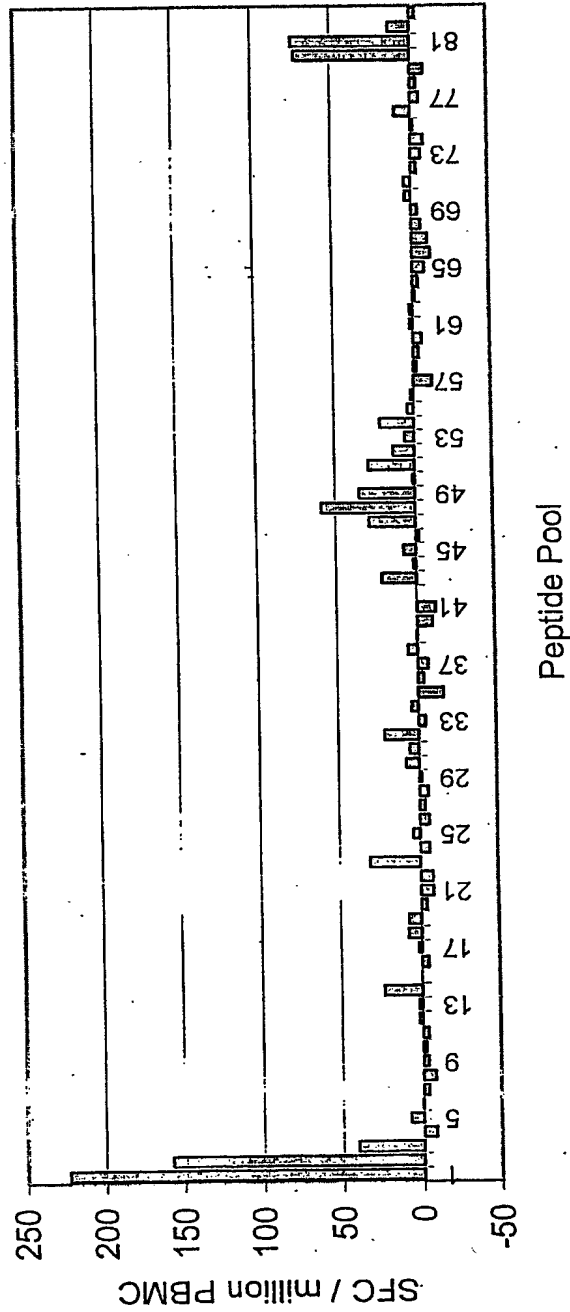
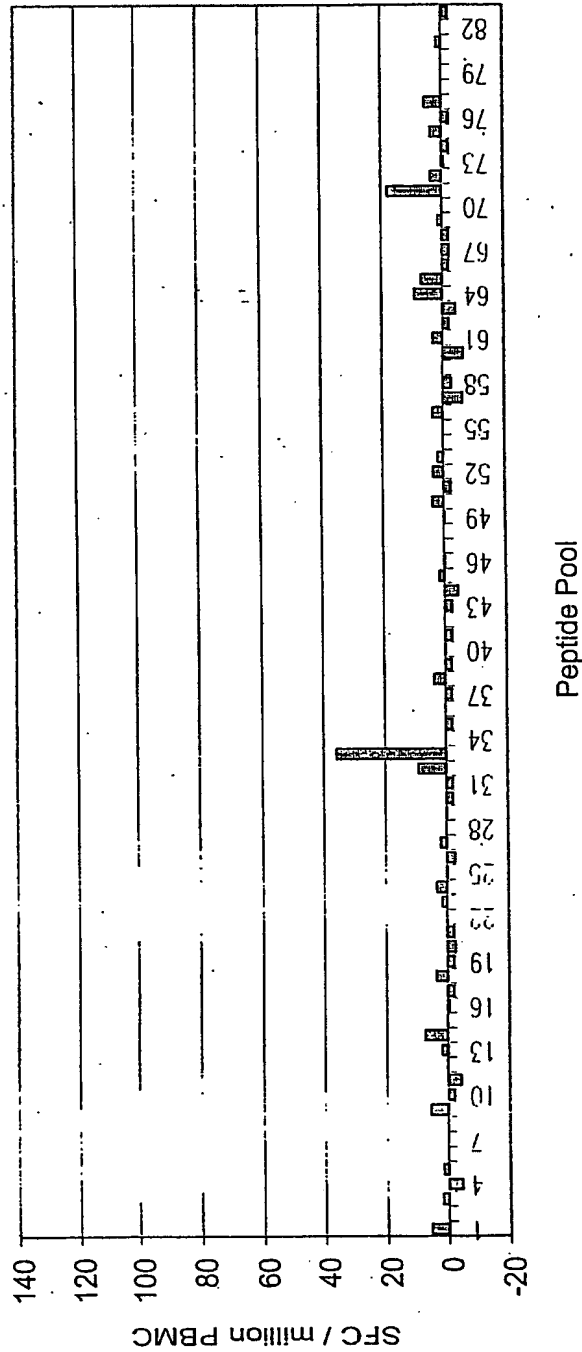


Figure 36. Coeliac HLA-DQ6/8 Subject C11: Change in IFNgamma ELISpot Responses to tTG-deamidated Gliadin Peptide Pools



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